Akebia Therapeutics, Inc. Form 424B5 March 22, 2018 Table of Contents

> Filed Pursuant to Rule 424(b)(5) Registration No. 333-223585

The information in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not offers to sell securities and we are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion, dated March 22, 2018

Preliminary Prospectus Supplement

(To Prospectus dated March 12, 2018)

\$85,000,000

Common Stock

We are offering \$85,000,000 of shares of our common stock pursuant to this prospectus supplement. Our common stock is listed for trading on The Nasdaq Global Market under the symbol AKBA. On March 21, 2018, the closing sales price of our common stock on The Nasdaq Global Market was \$12.00 per share.

We are an emerging growth company as defined by the Jumpstart Our Business Startups Act of 2012 and, as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus supplement and future filings.

Investing in our common stock involves a high degree of risk. See <u>Risk Factors</u> beginning on page S-5 of this prospectus supplement as well as the accompanying prospectus and the documents we have filed with the Securities and Exchange Commission that are incorporated by reference herein for more information before you make any investment in our common stock.

	Per share	Total
Public offering price	\$	\$
Underwriting discounts and commissions (1)	\$	\$
Proceeds, before expenses, to us	\$	\$

(1) We refer you to <u>Underwriting</u> beginning on page S-15 of this prospectus supplement for more information regarding underwriting compensation.

The underwriter may also purchase up to an additional \$12,750,000 of shares of common stock from us on the same terms and conditions as set forth above within 30 days from the date of this prospectus supplement. If the underwriter exercises the option in full, the total underwriting discounts and commissions will be \$ , and the total proceeds, before expenses, to us will be \$ .

Neither the Securities and Exchange Commission nor any state securities regulator has approved or disapproved these securities, or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The underwriter is offering the common stock set forth under Underwriting. Delivery of the shares will be made on our about , 2018.

Sole Book-Running Manager

**MORGAN STANLEY** 

The date of this prospectus supplement is , 2018.

## TABLE OF CONTENTS

# **Prospectus Supplement**

Presentation of Information	S-ii
Prospectus Supplement Summary	S-1
The Offering	S-3
Risk Factors	S-5
<u>Use of Proceeds</u>	S-6
Dividend Policy	S-7
Price Range of Our Common Stock	S-8
<u>Capitalization</u>	S-9
<u>Dilution</u>	S-10
Material United States Federal Income Tax Considerations for Non-U.S. Holders	S-11
Underwriting	S-15
Legal Matters	S-22
<u>Experts</u>	S-22
Where You Can Find More Information	S-22
Incorporation of Certain Information by Reference	S-22

# **Prospectus**

About This Prospectus	1
About Akebia Therapeutics, Inc.	2
Risk Factors	3
Cautionary Note Regarding Forward-Looking Statements	3
<u>Use of Proceeds</u>	4
Selling Securityholders	5
<u>Plan of Distribution</u>	6
<u>Description of Capital Stock</u>	7
<u>Description of Warrants</u>	11
<u>Description of Units</u>	12
Where You Can Find More Information	13
Incorporation of Certain Documents by Reference	13
<u>Legal Matters</u>	14
<u>Experts</u>	14

S-i

## PRESENTATION OF INFORMATION

These offering materials consist of two documents: (1) this prospectus supplement, which describes the terms of the common stock that we are currently offering, and (2) the accompanying prospectus, which provides general information about us. The information in this prospectus supplement supersedes any inconsistent information included or incorporated by reference in the accompanying prospectus.

Neither we nor the underwriter has authorized anyone to provide you with any additional information or any information that is different from that contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and any free writing prospectus provided in connection with this offering. We and the underwriter take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. Neither we nor the underwriter is making any offer to sell these securities in any jurisdiction where the offer or sale is not permitted. This prospectus supplement, the accompanying prospectus, any free writing prospectus provided in connection with this offering and the documents incorporated by reference herein and therein are accurate only as of their respective dates, regardless of the time of delivery of this prospectus supplement, the accompanying prospectus or any such free writing prospectus. Our business, operating results, financial condition and prospects may have changed since those dates.

It is important for you to read and consider all the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and any free writing prospectus provided in connection with this offering before making your investment decision.

This prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein and therein and any free writing prospectus provided in connection with this offering contain various forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the Securities Act ), and Section 21E of the Securities Exchange Act of 1934, as amended (the Exchange Act ), which represent our expectations or beliefs concerning future events. These forward-looking statements include, but are not limited to, statements about:

the potential therapeutic applications of the HIF pathway;

the potential of our pipeline and our research activities;

the potential therapeutic benefits, safety profile and effectiveness of our product candidates, including the potential for vadadustat to set a new standard of care in the treatment of anemia due to chronic kidney disease;

the potential indications and market potential and acceptance of our product candidates;

our competitive position, including estimates, developments and projections relating to our competitors and their products and product candidates, and our industry;

our expectations, projections and estimates regarding our costs, revenues, capital requirements, need for additional capital, cash flows, financial performance, profitability, tax obligations, liquidity, growth, contractual obligations, the period of time our cash resources and collaboration funding will fund our current operating plan, internal control over financial reporting, disclosure controls and procedures;

the timing of the availability and presentation of clinical trial data and results;

our and our collaborators strategy, plans and expectations with respect to the development, manufacturing, commercialization, launch, marketing and sale of our product candidates, and the associated timing thereof;

the designs of our studies, and the type of information and data expected from our studies;

the timing of or likelihood of regulatory filings and approvals, including labeling or other restrictions;

S-ii

the targeted timing of enrollment of our clinical trials;

the timing of initiation of our clinical trials and plans to conduct preclinical and clinical studies in the future;

the timing and amounts of payments from our collaborators and licensees, and the anticipated arrangements and benefits under our collaboration and license agreements;

our intellectual property position, including obtaining and maintaining patents; and the timing, outcome and impact of administrative, regulatory, legal and other proceedings relating to our patents and other proprietary and intellectual property rights;

the impact of accounting standards and estimates;

our facilities, lease commitments, and future availability of facilities;

our employees, employee compensation, and employee relations; and

the implementation of our business model and strategic plans for our business, product candidates and technology.

These forward-looking statements involve risks and uncertainties, including those that are described in Part I, Item 1A. Risk Factors included in our Annual Report on Form 10-K for the year ended December 31, 2017, filed with the Securities and Exchange Commission on March 12, 2018, and elsewhere in this prospectus supplement, that could cause our actual results, financial condition, performance or achievements to be materially different from those indicated in these forward-looking statements. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Forward-looking statements speak only as of the date that they are made. Except as required by law, we assume no obligation to publicly update or revise these forward-looking statements for any reason.

We own or have rights to trademarks, trade names and copyrights that we use in connection with the operation of our business, including our corporate names, logos and website names. Solely for convenience, some of the trademarks, trade names and copyrights referred to in this prospectus supplement are listed without the customary symbols, but we will assert, to the fullest extent permitted by applicable law, our rights to our trademarks, service marks, trade names and copyrights.

Unless stated otherwise or the context otherwise requires, we use the terms Akebia, the Company, we, us and outhis prospectus supplement to refer to Akebia Therapeutics, Inc. and its subsidiaries. When we refer to you we mean the investors and potential investors in the common stock offered hereby.

## PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information included or incorporated by reference in this prospectus supplement and the accompanying prospectus and does not contain all of the information that may be important to you. You should carefully review this entire prospectus supplement and the accompanying prospectus, including the risk factors and financial statements included and incorporated by reference in this prospectus supplement and the accompanying prospectus, before making your investment decision.

### **OUR BUSINESS**

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

HIF, a pathway involving hundreds of genes, is the same pathway used by the body to adapt to lower oxygen availability, or hypoxia, such as that experienced with a moderate increase in altitude. At higher altitudes, the body responds to lower oxygen levels by increasing the availability of HIF, which coordinates the interdependent processes of iron utilization and erythropoietin, or EPO, production to increase RBC production and, ultimately, improve oxygen delivery. The significance of the HIF pathway was recognized by the 2016 Albert Lasker Basic Medical Research Award, which honored the three physician-scientists who discovered the HIF pathway and elucidated this primary oxygen sensing mechanism that is essential for survival. HIF protein is constantly being produced under normal oxygen conditions, but is quickly degraded by prolyl hydroxylases, or PH. Under hypoxic conditions, HIF-PHs are inhibited, allowing HIF to stimulate erythropoiesis. These findings have opened up new possibilities for developing therapeutics, such as HIF-PH inhibitors, which have the potential to treat many diseases.

Our lead product candidate, vadadustat, is a HIF-PH inhibitor, or HIF-PHI, in Phase 3 development for the treatment of anemia due to CKD. Anemia is common in patients with CKD, and its prevalence increases as CKD progresses. Anemia is a condition characterized by abnormally low levels of hemoglobin. Hemoglobin is contained within RBCs and carries oxygen to other parts of the body. If there are too few RBCs or if hemoglobin levels are low, the cells in the body will not get enough oxygen. In patients with CKD, anemia results from inadequate EPO levels, which negatively affect RBC production. In addition, iron, which is essential to RBC production, may be deficient in patients with CKD. Left untreated, anemia significantly accelerates overall deterioration of patient health with increased morbidity and mortality.

Based on third party prevalence data and company estimates, approximately 37 million people in the United States have CKD and approximately 5.7 million of these individuals suffer from anemia. Anemia from CKD is currently treated by injectable recombinant human erythropoiesis-stimulating agents, or injectable ESAs, such as EPOGEN® (epoetin alfa) and Aranesp® (darbepoetin alfa), or with iron supplementation or RBC transfusion. Based on publicly available information on ESA sales and market data compiled by a third-party vendor, global sales of injectable ESAs for all uses were estimated to be approximately \$7.0 billion in 2016. The vast majority of these sales were for the treatment of anemia due to CKD.

When administered to a patient, injectable ESAs provide supra-physiological levels of exogenous erythropoietin to stimulate production of RBCs. While injectable ESAs can be effective in raising hemoglobin levels, they have the potential to cause significant side effects, and need to be injected subcutaneously or intravenously. In particular, injectable ESAs may lead to thrombosis, stroke, myocardial infarction and death. These safety concerns, which became evident starting in 2006, have led to a significant reduction in the use of injectable ESAs. Today, anemia is either not treated or inadequately treated in the majority of non-dialysis dependent, or NDD, CKD patients. There is an unmet need for treatment options that offer an improved safety profile and such agents would have significant market potential. Vadadustat is designed to stimulate erythropoiesis and effectively treat renal anemia while avoiding the supra-physiologic EPO levels previously observed with injectable ESAs. In addition, vadadustat, if approved, would provide patients with an oral treatment option, rather than an injection. For these reasons, we believe that vadadustat has the potential to set a new standard of care for the treatment of anemia due to CKD.

Phase 1 and Phase 2 data led us to the design of our Phase 3 clinical program for vadadustat. The vadadustat Phase 3 program in NDD-CKD patients with anemia, called PRO<sub>2</sub>TECT, and in dialysis dependent, or DD, CKD patients with anemia, called INNO<sub>2</sub>VATE, is designed to enroll up to approximately 6,900 patients evaluating once daily oral dosing of vadadustat against an injectable ESA active comparator, darbepoetin alfa. The enrollment numbers and the completion of PRO<sub>2</sub>TECT and INNO<sub>2</sub>VATE will be driven by the accrual of major adverse cardiovascular events, or MACE. In December 2015, the first patient was dosed in PRO<sub>2</sub>TECT, and the first patient was dosed in INNO<sub>2</sub>VATE in August 2016. As of December 31, 2017, we expect the remaining external aggregate contract research organization, or CRO, costs of PRO<sub>2</sub>TECT and INNO<sub>2</sub>VATE to be in the range of \$420.0 million to \$450.0 million. We anticipate reporting top-line clinical data for the PRO<sub>2</sub>TECT and INNO<sub>2</sub>VATE studies in 2019, subject to the accrual of MACE events. Subject to marketing approvals, we plan to launch vadadustat for the treatment of anemia due to CKD in 2020.

We revised the study designs of FO<sub>2</sub>RWARD and TRILO<sub>2</sub>GY, which we believe will provide additional characterization and differentiation of vadadustat and further strengthen our commercial position if our product candidate is approved. The revised FO<sub>2</sub>RWARD study will include once-daily and three-times weekly dosing, data to inform ESA-switching protocols, a larger sample size, and a broader dialysis population that is inclusive of hyporesponders, or patients with anemia due to CKD who are on dialysis and do not adequately respond to injectable ESA. Hyporesponders represent approximately 10-15% of subjects with anemia due to DD-CKD, yet they account for 30-40% of total injectable ESA use. These patients have demonstrated a persistently higher risk of mortality than non-hyporesponders, and represent a high unmet need. Given its differentiated mechanism of action, we believe that vadadustat may provide a treatment option for these patients. The revised TRILO<sub>2</sub>GY study will include once-daily and three-times weekly dosing and an ESA control, a larger sample size, and a design that can generate data to inform switching from Epogen<sup>®</sup>, Aranesp<sup>®</sup> and Mircera<sup>®</sup>.

If vadadustat is approved by the United States Food and Drug Administration, or FDA, we plan to establish our own commercial organization in the United States while leveraging our collaboration with Otsuka Pharmaceutical Co. Ltd., or Otsuka, and its well-established commercial organization in the United States. We also granted Otsuka exclusive rights to commercialize vadadustat in Europe, China and certain other markets, subject to marketing approvals. In Japan and certain other countries in Asia, we granted Mitsubishi Tanabe Pharma Corporation, or MTPC exclusive rights to commercialize vadadustat, subject to marketing approvals. In May 2017, we entered into an exclusive license agreement with Vifor (International) Ltd., or Vifor Pharma, to sell vadadustat solely to Fresenius Kidney Care Group LLC, or FKC, dialysis clinics in the United States subject to approval by the FDA and inclusion of vadadustat in a bundled reimbursement model. During the term of the license agreement, Vifor Pharma may not sell to FKC or its affiliates any HIF product that competes with vadadustat in the United States.

In addition to vadadustat, we are developing a HIF-based portfolio of product candidates that target serious diseases of high unmet need. Our portfolio includes product candidates developed internally as well as in-licensed product candidates, such as AKB-5169. In February 2017, we signed an exclusive agreement with Janssen Pharmaceutica NV, or Janssen, a subsidiary of Johnson & Johnson, for access to an extensive library of well-characterized HIF pathway compounds with potential applications across multiple therapeutic areas. The lead compound, AKB-5169, is a differentiated preclinical compound in development as an oral treatment for inflammatory bowel disease, or IBD. We intend to complete further preclinical development of this compound, and we are targeting submitting an Investigational New Drug application, or IND, to the FDA in 2018.

#### **OUR PRINCIPAL EXECUTIVE OFFICES**

Our principal executive offices are located at 245 First Street, Suite 1100, Cambridge, Massachusetts 02142. Our telephone number is (617) 871-2098. Our website address is www.akebia.com. The information found on our website, or that may be accessed by links on our website, is not part of this prospectus supplement or the accompanying prospectus.

#### **EMERGING GROWTH COMPANY**

We are an emerging growth company, as defined in the Jumpstart Our Business Startup Act of 2012. We will remain an emerging growth company until the earlier of (1) December 31, 2019 (the last day of the fiscal year following the fifth anniversary of our initial public offering), (2) the last day of the fiscal year in which we have total annual gross revenue of at least \$1.07 billion, (3) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th, and (4) the date on which we have issued more than \$1.07 billion in non-convertible debt during the prior three-year period. We refer to the Jumpstart Our Business Startup Act of 2012 herein as the JOBS Act, and references herein to emerging growth company shall have the meaning associated with it in the JOBS Act.

## THE OFFERING

The summary below describes the offering of our common stock. Certain of the terms and conditions described below are subject to important limitations and exceptions. The Description of Common Stock section of the accompanying prospectus contains a more detailed description of the terms and conditions of the common stock.

Common stock offered by Akebia

Common stock to be outstanding after this offering

\$85,000,000 of shares.

54,779,567 shares, which is based an aggregate offering of \$85,000,000 of our common stock at an assumed public offering price of \$11.86 per share, the last reported sale price of our common stock on The Nasdaq Global Market on March 20, 2018 (or 55,854,609 shares if the underwriter exercises its option to purchase additional shares).

Nasdaq Global Market symbol

**AKBA** 

**Use of proceeds**We intend to use the net proceeds from this offering for

the continued clinical development and optimization of the vadadustat program, including pre-commercial planning activities, and the remainder for working capital, business development and other general

corporate purposes. See Use of Proceeds.

Risk factors

See Risk Factors beginning on page S-5 of this prospectus supplement, as well as the accompanying prospectus and the documents we have filed with the Securities and Exchange Commission (the SEC ) that are incorporated by reference herein and therein.

The number of shares of common stock to be outstanding after this offering is based on 47,612,619 shares outstanding as of December 31, 2017 and excludes:

3,660,014 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2017 at a weighted-average exercise price of \$9.47 per share and 728,738 shares of common stock issuable upon vesting of restricted stock units as of December 31, 2017;

1,790,600 shares of common stock reserved for future issuance under our 2014 Incentive Plan, 652,290 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan and 750,000 shares of common stock reserved for issuance in 2018 under our Inducement Award Program; and

509,611 shares of common stock reserved for future issuance pursuant to outstanding warrants at an exercise price of \$9.81 per share.

Except as otherwise indicated, all information contained in this prospectus:

assumes that the underwriter does not exercise its option to purchase additional shares; and

assumes no exercise of outstanding options or warrants or vesting of restricted stock units after December 31, 2017.

## **RISK FACTORS**

An investment in our common stock involves risks. You should carefully consider the risks described below, as well as the other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus, including Part I, Item IA Risk Factors in our Annual Report on Form 10-K for the year ended December 31, 2017, filed with the SEC on March 12, 2018, before making an investment decision. In addition, please read Presentation of Information in this prospectus supplement and Cautionary Note Regarding Forward-Looking Statements in the accompanying prospectus, where we describe additional uncertainties associated with our business and the forward-looking statements included or incorporated by reference in this prospectus supplement and the accompanying prospectus. Please note that additional risks not currently known to us or that we currently deem immaterial may also impair our business and operations.

## Risks Related to this Offering

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

The 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 as adjusted net tangible book value per share after this offering. To the extent shares subsequently are issued upon the exercise of options or warrants or the vesting of restricted stock units, you will incur further dilution. Based on an assumed public offering price of \$11.86 per share, the last reported sale price of our common stock on The Nasdaq Global Market on March 20, 2018, you will incur immediate and substantial dilution of \$8.13 per share, representing the difference between our as adjusted net tangible book value per share, after giving effect to this offering, and the public offering price. See the section of this prospectus supplement entitled Dilution for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

#### 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 the continued clinical development and optimization of the vadadustat program, including pre-commercial planning activities, and the remainder for working capital, business development and other general corporate purposes. See the section of this prospectus supplement entitled Use of Proceeds for further detail. 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.

S-5

## **USE OF PROCEEDS**

We estimate that the net proceeds from this offering will be approximately \$84.8 million (or approximately \$97.5 million if the underwriter exercises its option to purchase additional shares in full), after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering for the continued clinical development and optimization of the vadadustat program, including pre-commercial planning activities, and the remainder for working capital, business development and other general corporate purposes.

Our expected use of net proceeds from this offering represents our intentions based on our present plans and business conditions, which could change as our plans and business conditions evolve. The amount and timing of our actual expenditures will depend on 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 our use of the net proceeds from this offering, we may temporarily invest the net proceeds in investment-grade, interest-bearing securities.

We anticipate that the net proceeds from this offering, together with our existing cash and cash equivalents, available for sale securities and the funds expected to be received in connection with our collaborations, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into the first quarter of 2020. We have based these estimates on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

S-6

## **DIVIDEND POLICY**

We have not paid cash dividends on our common stock during our two most recent fiscal years. We do not intend to pay any dividends on our common stock for the foreseeable future.

S-7

## PRICE RANGE OF OUR COMMON STOCK

Our common stock has been publicly traded on The Nasdaq Global Market under the symbol AKBA since our initial public offering on March 19, 2014. The following table summarizes the high and low sale prices for our common stock for the fiscal periods indicated as reported on The Nasdaq Global Market.

	High	Low
2016		
First Quarter	\$12.74	\$ 7.02
Second Quarter	\$ 9.99	\$ 7.00
Third Quarter	\$ 9.38	\$ 7.31
Fourth Quarter	\$11.07	\$ 7.16
2017		
First Quarter	\$ 10.70	\$ 8.58
Second Quarter	\$ 16.54	\$ 8.69
Third Quarter	\$ 19.73	\$12.78
Fourth Quarter	\$ 20.25	\$ 14.07
2018		
First Quarter (through March 20, 2018)	\$ 15.86	\$11.71

On March 20, 2018, the last reported sale price for our common stock on The Nasdaq Global Market was \$11.86 per share. As of March 1, 2018, we had 22 stockholders of record.

## **CAPITALIZATION**

The following table sets forth our cash and cash equivalents, available for sale securities and capitalization as of December 31, 2017:

on an actual basis; and

on an as adjusted basis to reflect the sale of shares of common stock in this offering and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us and based on an assumed public offering price of \$11.86 per share, the last reported sale price of our common stock on The Nasdaq Global Market on March 20, 2018.

You should read the following table along with our financial statements and the accompanying notes to those statements.

	As of December 31, 2017	
	Actual	As Adjusted
Cash and cash equivalents and available for sale securities	\$ 317,791,800	\$ 402,567,800
Stockholders equity (deficit):		
Preferred stock, \$0.00001 par value; 25,000,000 shares authorized, none		
issued and outstanding		
Common stock, \$0.00001 par value; 175,000,000 shares authorized,		
47,612,619 shares issued and outstanding actual; and 54,779,567 shares issued		
and outstanding, as adjusted	474	546
Additional paid-in capital	493,822,522	578,598,451
Accumulated other comprehensive income (loss)	(441,601)	(441,601)
Accumulated deficit	(374,049,953)	(374,049,953)
Total stockholders equity	119,331,443	204,107,443
Total capitalization	\$ 119,331,443	\$ 204,107,443

The number of shares of common stock to be outstanding after this offering is based on 47,612,619 shares outstanding as of December 31, 2017 and excludes:

3,660,014 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2017 at a weighted-average exercise price of \$9.47 per share and 728,738 shares of common stock issuable upon vesting of restricted stock unites as of December 31, 2017;

1,790,600 shares of common stock reserved for future issuance under our 2014 Incentive Plan, 652,290 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan and 750,000 shares of common stock reserved for issuance in 2018 under our Inducement Award Program; and

509,611 shares of common stock reserved for future issuance pursuant to outstanding warrants at an exercise price of \$9.81 per share.

S-9

#### **DILUTION**

If you invest in our common stock, your interest will be diluted to the extent of the difference between the price per share you pay in this offering and the net tangible book value per share of our common stock immediately after this offering. Our net tangible book value of our common stock as of December 31, 2017 was approximately \$119.3 million, or approximately \$2.51 per share of common stock based on 47,612,619 shares outstanding as of December 31, 2017. Net tangible book value per share is equal to our total tangible assets, less our total liabilities, divided by the total number of shares outstanding as of December 31, 2017.

After giving effect to the sale by us of \$85,000,000 of common stock at an assumed offering price of \$11.86 per share, the last reported sale price of our common stock on The Nasdaq Global Market on March 20, 2018, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2017 would have been approximately \$204.1 million, or \$3.73 per share. This would represent an immediate increase in net tangible book value of \$1.22 per share to our existing stockholders and an immediate dilution in net tangible book value of \$8.13 per share to new investors purchasing our common stock in this offering at the assumed public offering price. The following table illustrates this calculation on a per share basis:

Assumed offering price per share	\$ 11.86
Net tangible book value per share as of December 31, 2017	2.51
Increase in net tangible book value per share attributable to the offering	1.22
As adjusted net tangible book value per share after giving effect to the offering	3.73
Dilution in net tangible book value per share to new investors in the offering	\$ 813

The information discussed above is illustrative only and will adjust based on the actual public offering price and other terms of this offering determined at pricing.

The foregoing table and discussion is based on 47,612,619 shares outstanding as of December 31, 2017 and excludes:

3,660,014 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2017 at a weighted-average exercise price of \$9.47 per share and 728,738 shares of common stock issuable upon vesting of restricted stock units as of December 31, 2017;

1,790,600 shares of common stock reserved for future issuance under our 2014 Incentive Plan, 652,290 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan and 750,000 shares of common stock reserved for issuance in 2018 under our Inducement Award Program; and

509,611 shares of common stock reserved for future issuance pursuant to outstanding warrants at an exercise price of \$9.81 per share.

The exercise of outstanding options to purchase shares of our common stock having an exercise price less than the public offering price would increase the dilutive effect to new investors.

This discussion of dilution, and the table quantifying it, assumes no issuance of up to \$12.8 million in shares of common stock that we may sell to the underwriter upon exercise of its option to purchase additional shares. If the underwriter exercises in full its option to purchase additional shares at the assumed public offering price of \$11.86 per share, the last reported sale price of our common stock on The Nasdaq Global Market on March 20, 2018, the as adjusted net tangible book value after this offering would be approximately \$3.88 per share, representing an increase in net tangible book value of approximately \$1.38 per share to existing stockholders and immediate dilution in net tangible book value of approximately \$7.98 per share to investors purchasing our common stock in this offering at the public offering price.

S-10

## 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 shares of our common stock acquired pursuant to this offering 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 with respect to shares of our common stock. This summary is based upon the U.S. Internal Revenue Code of 1986, as amended (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 change or differing interpretations at any time, possibly with retroactive effect.

This summary assumes that shares of our common stock are held by a Non-U.S. Holder 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 who are subject to special treatment under U.S. federal income tax laws (including, for example, financial institutions, broker-dealers, insurance companies, partnerships or other pass-through entities or arrangements, certain U.S. expatriates or former long-term residents of the United States, tax-exempt organizations, pension plans, controlled foreign corporations and passive foreign investment companies (each as defined in the Code), 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 shares of our 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% 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 arising 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 shares of our common stock that, for U.S. federal income tax purposes, is an individual, corporation, estate or trust other than:

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, that is 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 United States persons (as defined in the Code) 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 United States person.

A modified definition of Non-U.S. Holder applies for U.S. federal estate tax purposes (as discussed below).

If an entity that is classified as a partnership for U.S. federal income tax purposes holds shares of 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. Partnerships and other entities that are classified as partnerships for U.S. federal income tax purposes that hold shares of our common stock and their investors are urged to consult their tax advisors.

There can be no assurance that the 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 or an opinion of counsel with

S-11

respect to the U.S. federal income or estate tax consequences to a Non-U.S. Holder of the purchase, ownership or disposition of shares of our common stock.

THIS SUMMARY IS FOR GENERAL INFORMATION ONLY AND IS NOT INTENDED TO BE TAX ADVICE. PROSPECTIVE INVESTORS ARE URGED TO CONSULT THEIR TAX ADVISORS CONCERNING THE U.S. FEDERAL INCOME AND ESTATE TAX CONSEQUENCES TO THEM OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF SHARES OF OUR COMMON STOCK, AS WELL AS THE APPLICATION OF STATE, LOCAL AND NON-U.S. INCOME TAX AND OTHER TAX LAWS.

#### **Distributions on Shares of Our Common Stock**

As discussed under Dividend Policy above, we do not currently pay, and do not anticipate paying in the foreseeable future, cash dividends on shares of our common stock. In the event that we do make a distribution of cash or property with respect to shares of our common stock, any such distributions generally will constitute dividends for U.S. federal income tax purposes to the extent of our current or accumulated earnings and profits, as determined under U.S. federal income tax principles, and will be subject to withholding as described in the next paragraph below. If a distribution exceeds our current or accumulated earnings and profits, the excess will be treated as a tax-free return of the Non-U.S. Holder s investment, up to such holder s adjusted tax basis in its shares of our common stock. 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 shares of Our Common Stock. Any distribution described in this paragraph would also be subject to the discussion below in Additional Withholding and Information Reporting Requirements for Shares of Our Common Stock Held by or through Non-U.S. Entities.

Any dividends paid to a Non-U.S. Holder with respect to shares of our common stock generally will be subject to a 30% U.S. federal withholding tax unless such Non-U.S. Holder provides the applicable withholding agent with an appropriate and validly completed IRS Form W-8 (including applicable attachments) establishing a reduction or exemption from such withholding tax (which form may be required to be updated periodically), prior to the payment of dividends, such as:

IRS Form W-8BEN or W-8BEN-E, as appropriate (or successor form), certifying, under penalties of perjury, that such Non-U.S. Holder is entitled to a reduction in withholding under an applicable income tax treaty; or

IRS Form W-8ECI (or successor form) certifying, under penalties of perjury, that a dividend paid on shares of our common stock is not subject to withholding tax because it is effectively connected with the conduct of 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. federal income tax rates on a net income basis as described below).

The certification requirement described above also may require a Non-U.S. Holder that provides an IRS form or that claims treaty benefits to provide its U.S. taxpayer identification number. Special certification and other requirements apply in the case of certain Non-U.S. Holders that are intermediaries or pass-through entities for U.S. federal income tax purposes.

Each Non-U.S. Holder is urged to consult its 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 the conduct of a trade or business in the United States of the Non-U.S. Holder (and, if required by an applicable income tax treaty, are attributable to a permanent establishment or fixed base maintained by such Non-U.S. Holder in the United States), the Non-U.S. Holder, although exempt from the withholding tax described above (provided that the certifications described above are

S-12

satisfied), will generally 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 resident of the United States. In addition, if a dividend is received by a Non-U.S. Holder taxable as a corporation for U.S. federal income tax purposes, such Non-U.S. Holder may be subject to an additional branch profits tax at a 30% rate, unless an applicable income tax treaty provides otherwise.

If a Non-U.S. Holder is eligible for a reduced rate of U.S. federal withholding tax pursuant to an applicable income tax treaty, such holder may obtain a refund or credit of any excess amount withheld by timely filing an appropriate claim for refund with the IRS.

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

Subject to the discussion below under Additional Withholding and Information Reporting Requirements for Shares of Our Common Stock Held by or through Non-U.S. Entities, in general, a Non-U.S. Holder will not be subject to U.S. federal income tax or withholding tax on any 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 with respect to the applicable shares of our common stock (the relevant period), 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% (unless an applicable income tax treaty provides otherwise) 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.

With respect to the second exception above, although there can be no assurance, we believe we are not, and we do not currently 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 relative to the fair market value of other business assets, there can be no assurance that we are not currently or will not become a USRPHC in the future. Generally, a corporation is a USRPHC only if the fair market value of its United States 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 certain other assets used or held for use in a trade or business. Even if we are or become 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 shares of our common stock by reason of our status as a USRPHC so long as (i) our common stock is regularly traded on an established securities market (within the meaning of Code Section 897(c)(3)) during the calendar year in which such sale, exchange or other taxable disposition of shares of our common stock occurs and (ii) such Non-U.S. Holder does not own and is not deemed to own (directly, indirectly or constructively) more than 5% of our common stock at any time during the relevant period. If we are a USRPHC and the requirements of (i) or (ii) are not met, gain on the disposition of shares of our common stock generally will be taxed in the same manner as gain that is effectively connected with the conduct of a U.S. trade or business, except that the branch profits tax generally will not apply to gain from the disposition of stock in a USRPHC. Prospective investors are urged to consult their tax advisors regarding the possible consequences to them if we are, or were to become, a USRPHC.

If the third exception applies, the Non-U.S. Holder generally will be subject to U.S. federal income tax on a net income basis with respect to such gain in the same manner as if such holder were a resident of the United States,

unless otherwise provided in an applicable income tax treaty, 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 on its effectively connected earnings and profits at a rate of 30%, unless an applicable income tax treaty provides otherwise.

S-13

# Additional Withholding and Information Reporting requirements for Shares of Our Common Stock Held by or through Non-U.S. Entities

Sections 1471 through 1474 of the Code and related Treasury regulations and guidance (commonly referred to as FATCA) generally will impose a U.S. federal withholding tax of 30% on certain payments to certain non-U.S. entities (including certain intermediaries), including dividends on and the gross proceeds from a sale, exchange, or other disposition of shares of our common stock, unless such persons comply with a complicated U.S. information reporting, disclosure and certification regime. This regime requires, among other things, a broad class of persons to enter into agreements with the IRS to obtain, disclose and report information about their investors and account holders. An intergovernmental agreement between the United States and an applicable foreign country may, however, modify these requirements and these requirements are different from and in addition to the certification requirements described elsewhere in this discussion. The FATCA withholding rules currently apply to dividend payments on our common stock and are scheduled to apply to payments of gross proceeds from the sale or other disposition of shares of our common stock occurring after December 31, 2018. Prospective investors should consult their 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**

Payors generally must report annually to the IRS and to each Non-U.S. Holder the gross amount of the distributions on shares of our common stock paid to such holder and the tax withheld, if any, with respect to such d