

Aeglea BioTherapeutics, Inc.
Form 424B4
April 07, 2016
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Filed Pursuant to Rule 424(b)(4)
Registration No. 333-205001

PROSPECTUS

5,000,000 Shares

Common Stock

This is the initial public offering of our common stock. We are offering 5,000,000 shares of common stock. Prior to this offering, there has been no public market for our common stock. We have been approved to list our common stock on The NASDAQ Global Market under the symbol AGLE. The public offering price is \$10.00 per share.

We are an emerging growth company under applicable Securities and Exchange Commission rules and will be eligible for, and have decided to comply with, reduced public company disclosure requirements.

Our business and an investment in our common stock involve significant risks. These risks are described under the caption Risk Factors beginning on page 11 of this prospectus.

	<i>Per Share</i>	<i>Total</i>
Public Offering Price	\$ 10.00	\$ 50,000,000
Underwriting Discount(1)	\$ 0.70	\$ 3,500,000
Proceeds to Aeglea BioTherapeutics (Before Expenses)	\$ 9.30	\$ 46,500,000

(1) We refer you to Underwriting beginning on page 146 of this prospectus for additional information regarding total underwriter compensation.

Certain of our existing stockholders or their affiliates have agreed to purchase an aggregate of approximately 3,175,000 shares of our common stock in this offering at the initial public offering price. The underwriters will receive the same underwriting discount on the shares purchased by these parties as they will on the other shares sold to the public in this offering. See Summary Insider Participation.

We have granted the underwriters an option for a period of 30 days to purchase up to an additional 750,000 shares of common stock.

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

Delivery of the shares of our common stock is expected to be made on or about April 12, 2016.

UBS Investment Bank

**BMO Capital Markets
Needham & Company**

Wells Fargo Securities

The date of this prospectus is April 6, 2016

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We have not, and the underwriters have not, authorized anyone to provide any information or to make any representations other than those contained in this prospectus or in any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus or in any applicable free writing prospectus is current only as of its date, regardless of its time of delivery or any sale of shares of our common stock. Our business, financial condition, results of operations and prospectus may have changed since that date.

Neither we nor the underwriters have done anything that would permit this offering, or possession or distribution of this prospectus, in any jurisdiction where action for that purpose is required, other than in the United States. Persons who come into possession of this prospectus and any applicable free writing prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus and any such free writing prospectus applicable to that jurisdiction.

(i)

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PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in 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 consolidated financial statements and the related notes thereto and the information set forth under the sections Risk Factors and Management's Discussion and Analysis of Financial Condition and Results of Operations, in each case included in this prospectus. Unless the context otherwise requires, we use the terms Aeglea, Aeglea BioTherapeutics, company, we, us and our in this prospectus to refer to Aeglea BioTherapeutics, Inc. and our consolidated subsidiaries.

Overview

We are a biotechnology company committed to developing enzyme-based therapeutics in the field of amino acid metabolism that we believe will transform the lives of patients with inborn errors of metabolism and cancer. Our engineered human enzymes are designed to degrade specific amino acids in the blood. In inborn errors of metabolism, or IEM, a subset of rare genetic metabolic diseases, we are seeking to reduce toxic levels of amino acids in patients. In oncology, we are seeking to reduce amino acid blood levels below the normal range, where we believe we will be able to exploit the dependence of certain cancers on specific amino acids.

Our lead product candidate, AEB1102, is engineered to degrade the amino acid arginine and is being developed to treat two extremes of arginine metabolism, including arginine excess in patients with Arginase I deficiency, an IEM, as well as some cancers which have been shown to have a metabolic dependence on arginine. Arginine is an amino acid involved in many biochemical functions in the body. AEB1102 has demonstrated the ability to reduce blood arginine levels in clinical and nonclinical studies, supporting its potential use as a treatment of both Arginase I deficiency and cancer. We have an effective investigational new drug application, or IND, with the U.S. Food and Drug Administration, or FDA, for AEB1102 for the treatment of solid tumors. In October 2015, we initiated enrollment for this dose escalation trial in patients with advanced solid tumors. We have since treated our first two cohorts of seven patients total, and a temporary reduction of blood arginine was observed, providing initial human proof of mechanism for AEB1102. We have an effective IND and plan to initiate a Phase 1 dose escalation trial in patients with hematological malignancies in the first half of 2016. We plan to initiate expansion trials in patients with solid tumors and an additional Phase 1 trial in combination with the standard of care in one or more solid tumor types in 2017. We have an effective IND for a Phase 1 dose escalation study in adult Arginase I deficiency patients and anticipate starting enrollment in the first half of 2016. We anticipate submitting a clinical trial application, or CTA, to the European Medicines Agency, or EMA, in the second half of 2016 for a Phase 2 trial in Arginase I deficiency patients and expect to initiate that trial in the first half of 2017. We are also building a pipeline of additional product candidates targeting key amino acids formed in or necessary for metabolism, or metabolites. These targets include the amino acid homocystine, a target for another IEM, as well as the amino acids cysteine/cystine and the amino acid methionine in oncology. Our current product candidates have been in-licensed from the University of Texas at Austin or assigned to us from one of our founders. We retain global commercialization rights for all of our product candidates.

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The following table summarizes our product candidate pipeline:

Our Focus

Our company was founded to develop therapeutics characterized by abnormal amino acid metabolism. An in-depth understanding of abnormal metabolic pathways is crucial to developing therapies that may address various disease states, including IEM and cancer.

Inborn errors of metabolism background

Enzymatic defects in metabolic processes contribute to a class of genetic diseases known as IEM. We focus on those IEM that are characterized by excess levels of amino acids and other metabolites that become toxic to patients. In these circumstances, we expect patients to benefit from reduced levels of the target amino acid or metabolite to a normal concentration range. We believe this can be successfully achieved through our enzyme replacement therapy.

Cancer background and abnormal metabolism

We believe that the altered metabolism of cancer cells the atypical uptake and break down of nutrients provides an opportunity to develop important new cancer treatments. It is our belief that depriving cancer cells of key amino acids that are essential for cell survival and tumor growth will provide an effective treatment for some cancers.

Enzyme-based therapies that degrade amino acids have shown clinical benefit in the treatment of cancer. However, some microbial-derived enzymes, derived from microorganisms like bacteria, may have limited clinical utility due to the patients immunological reaction to these agents. We expect that our enzyme product candidates, which are engineered from human proteins, will be less likely to elicit an immune response, a defense function of the body to protect against invading pathogens or foreign tissues, as compared to microbial enzymes and should provide greater flexibility with respect to the target amino acids that can be addressed to treat disease.

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By depriving cancer cells of these amino acids via our engineered human enzyme product candidates, we provide a novel approach that, when used alone or in combination with existing or emerging standards of care, has the potential to be an effective treatment paradigm for cancer patients.

The Aeglea Approach

We apply our cellular metabolism expertise to build a portfolio of engineered human enzyme therapeutics that target distinct metabolites and provide additional therapeutic options for IEM and cancer. We identify new targets for enzyme therapeutics by leveraging scientific and medical literature and available clinical precedents. We use protein engineering techniques to create enzymes displaying the requisite catalytic and pharmacological properties that can degrade these targets and effectively address the metabolic defects observed in IEM or the dependence of certain cancers on amino acids or other metabolites. Certain metabolites require modified enzymes to properly control their levels in a therapeutic setting. We engineer human proteins as scaffolds to develop therapeutic products and to help avoid the immunogenicity problems, or the likelihood to cause an immune response, seen with non-human protein-based drugs. Our goal is to create engineered human enzymes with the appropriate properties to be developed into effective and well-tolerated therapeutics.

An integral component of our product development programs is the integration of a precision medicine strategy utilizing biomarkers to identify patients who are most likely to benefit from our product candidates. The identification of a target patient population may potentially lead to proof-of-concept earlier in clinical development. We believe this approach will lead to a more efficient regulatory strategy and a higher likelihood of demonstrating clinical benefit.

Our Development Programs

AEB1102

AEB1102 is human Arginase I, engineered to reduce arginine levels to treat both patients with Arginase I deficiency and patients with arginine-dependent solid tumors and hematological malignancies.

Arginase I has been investigated extensively as a method for reducing arginine levels. Native human Arginase I, however, is not an ideal therapeutic candidate due to low catalytic activity and poor stability under physiological conditions. To support its development as a product candidate, we have improved on the catalytic activity and stability of human Arginase I, providing increased potency in both *in vitro* and *in vivo* models.

AEB1102 background in Arginase I deficiency and clinical development

Arginase I deficiency is a rare genetic disorder caused by a mutation in the Arginase I gene, ARG1, which leads to the inability to degrade arginine. Patients with this disease are predisposed to neurologic symptoms, including cognitive deficits and seizures, and frequently suffer from spasticity, loss of ambulation and severe intellectual disability. There is no approved therapeutic agent that addresses the cause of Arginase I deficiency, although the medical literature suggests that disease progression can be slowed with strict adherence to dietary protein restriction.

AEB1102 is intended to replace the function of Arginase I in patients, and return elevated arginine levels to the normal physiological range. Normalization of arginine levels is anticipated to slow or halt the progression of disease in these patients.

We have obtained orphan drug designation in the United States for AEB1102 for the treatment of patients with Arginase I deficiency. The FDA may grant orphan drug designation for drugs or biologics designed to treat disorders

affecting fewer than 200,000 people in the United States. We have an

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effective IND for a Phase 1 dose escalation study in adult Arginase I deficiency patients and anticipate starting enrollment in the first half of 2016. Additionally, we plan to initiate a Phase 2 trial in the first half of 2017 in Europe in up to ten patients with Arginase I deficiency. If the results from this trial are supportive, we anticipate initiating a randomized Phase 3 trial, enrolling approximately 15-30 patients in the United States and Europe that, if successful, will support a Biologics License Application, or BLA, filing with the FDA and a Marketing Authorization Application, or MAA, with the EMA. If the data from the Phase 1 trial are supportive, we may seek to accelerate our development plan for AEB1102 by requesting to use established regulatory pathways, such as Breakthrough Therapy and Fast Track designations.

AEB1102 background in oncology and clinical development

We are planning to target the dependence of some cancers on the amino acid arginine using AEB1102. Arginine is considered a semi-essential amino acid since in some circumstances cells cannot produce sufficient amounts of arginine. These circumstances include conditions of enhanced proliferation, tissue injury or stress.

Many types of cancers lose the ability to synthesize intracellular arginine, principally due to deficiency in the expression of any one or more of the following enzymes: ornithine transcarbamoylase, or OTC, argininosuccinate synthase, or ASS, and argininosuccinate lyase, or ASL. As a result, these cancers depend on extracellular arginine uptake. When deprived of this tumor-essential nutrient, cancer cells die, establishing a correlation between their inability to synthesize arginine and vulnerability to arginine deprivation. As documented in scientific and medical literature and from our own nonclinical research, the lack of expression of any one or more of the enzymes OTC, ASS or ASL in tumor cells has been shown to be a predictive biomarker for arginine dependent cancer cells.

For our IND in solid tumors that became effective in September 2015, we initiated enrollment and treated our first two cohorts of seven patients total in a Phase 1 trial in solid tumors with two stages: dose escalation and expansion. We have an effective IND and plan to initiate an additional Phase 1 trial for hematological malignancies in the first half of 2016. At the end of our Phase 1 dose escalation in solid tumors, we intend to initiate expansion arms in different tumor types in 2017. Also in 2017, we plan to initiate an additional Phase 1 trial, which will evaluate AEB1102 in combination with the standard of care in one or more solid tumor types.

Additional pipeline opportunities

In addition to AEB1102, we have identified several other target amino acids that we believe will have clinical relevance in the treatment of IEM and cancer. Our pipeline of engineered human enzyme product candidates in nonclinical development includes: AEB4104, an engineered human enzyme to target the reduction of elevated levels of the amino acid homocystine associated with the IEM classical homocystinuria; AEB3103, a cysteine/cystine degrading enzyme to target a widely recognized but previously unexploited vulnerability of cancer to oxidative stress; and AEB2109, a methionine degrading enzyme to target the methionine dependence of some cancers. We plan to continue nonclinical development of AEB4104, AEB3103, AEB2109 and related variants of these candidates. In addition, our ongoing research efforts have identified opportunities to leverage our expertise in the field of enzyme biochemistry to develop product candidates targeting various IEM and tumor metabolism mechanisms.

Our Strategy

Our goal is to build a fully integrated biotechnology company dedicated to the development and commercialization of engineered human enzymes targeting abnormal metabolism to transform the lives of patients. To execute our strategy, we intend to:

n successfully advance our lead product candidate, AEB1102, through clinical development;

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- n target enzyme-based therapeutic opportunities within IEM and oncology that have defined mechanisms of action and known disease pathways;
- n develop a precision medicine strategy that increases the probability of clinical success;
- n concurrently develop multiple product candidates; and
- n seek global approval and commercialization of our product candidates.

Risks Affecting Us

Our business is subject to a number of risks and uncertainties, including those highlighted in the section titled Risk Factors immediately following this prospectus summary. Some of these risks are:

- n 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;
- n we have no source of product revenue, have incurred significant losses since inception, and expect to incur losses for the foreseeable future and may never achieve or maintain profitability;
- n we may not be successful in advancing the clinical development of our product candidates, including AEB1102, or we or third parties may not be successful in developing companion diagnostics for our product candidates;
- n we will need substantial additional funding, and if we are unable to raise capital when needed, we would be compelled to delay, reduce or eliminate our product development programs or commercialization efforts;
- n we depend heavily on the success of our most advanced product candidate, AEB1102;
- n we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any of our product candidates, all of which are still in nonclinical development or nonclinical testing;
- n we may not be able to submit INDs, or the foreign equivalent outside of the United States, to commence clinical trials for product candidates on the timeframes we expect, and even if we are able to, the FDA or comparable foreign regulatory authorities may not permit us to proceed with planned clinical trials;
- n we have only very recently initiated enrollment for our Phase 1 clinical trial for the treatment of solid tumors for AEB1102 and treated our first two cohorts of seven patients total, and we have not dosed any of our other product candidates in humans; our planned clinical trials may reveal significant adverse events, toxicities or other side effects not seen in our nonclinical studies and may result in a safety profile that could inhibit regulatory approval or market acceptance of any of our product candidates;
- n if we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired;
- n our engineered human enzyme product candidates for our oncology indications represent a novel approach to cancer treatment, which could result in heightened regulatory scrutiny, delays in clinical development, or delays in our ability to achieve regulatory approval or commercialization of our product candidates; and
- n if we experience delays or difficulties in the enrollment of patients in our planned clinical trials, especially for AEB1102 for Arginase I deficiency where potential patients are rare, our receipt of necessary regulatory approvals could be delayed or prevented.

Corporate Information

We were formed as a limited liability company under the laws of the State of Delaware in December 2013 and converted to a Delaware corporation in March 2015. In connection with our conversion to a Delaware corporation, each of our outstanding shares of the members of the limited liability company was converted into shares of capital stock. On the date of conversion, each Series A convertible preferred

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share converted into a share of Series A convertible preferred stock, and each Common A share, Common A-1 share and Common B share converted into shares of common stock.

Our principal executive offices are located at 901 S. MoPac Expressway, Barton Oaks Plaza One, Suite 250, Austin, Texas 78746, and our telephone number is (512) 942-2935. Our website address is www.aegleabio.com. The information contained on, or that can be accessed through, our website is not part of this prospectus. Investors should not rely on any such information in deciding whether to purchase our common stock.

The Aeglea design logo, Aeglea BioTherapeutics and our other trade names, trademarks and service marks are the property of Aeglea BioTherapeutics, Inc. This prospectus contains additional trade names, trademarks and service marks of other companies. We do not intend our use or display of other companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies.

Implications of Being an Emerging Growth Company

As a company with less than \$1.0 billion in revenue during our last fiscal year, we qualify as an emerging growth company as defined in the Jumpstart Our Business Startups Act, or the JOBS Act, enacted in April 2012. An emerging growth company may take advantage of reduced reporting requirements that are otherwise applicable to public companies. These provisions include, but are not limited to:

- n being permitted to present only two years of audited financial statements and only two years of related Management's Discussion and Analysis of Financial Condition and Results of Operations in this prospectus;
- n not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended;
- n reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and
- n exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may use these provisions until the last day of our fiscal year following the fifth anniversary of the closing of our initial public offering. However, if certain events occur prior to the end of such five-year period, including if we become a large accelerated filer, our annual gross revenue exceed \$1.0 billion or we issue more than \$1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to the end of such five-year period.

We have elected to take advantage of certain of the reduced disclosure obligations in the registration statement of which this prospectus is a part and may elect to take advantage of other reduced reporting requirements in future filings. As a result, the information that we provide to our stockholders may be different than you might receive from other public reporting companies in which you hold equity interests.

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. 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.

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THE OFFERING

Common stock offered by us	5,000,000 shares
Common stock to be outstanding after this offering	12,929,832 shares
Option to purchase additional shares	We have granted the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to 750,000 additional shares of common stock.
Use of proceeds	<p>We estimate that we will receive net proceeds of approximately \$42.6 million (or approximately \$49.6 million if the underwriters option to purchase additional shares is exercised in full) from the sale of the shares of common stock offered by us in this offering, based on the initial public offering price of \$10.00 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.</p> <p>We intend to use the net proceeds from this offering for the following purposes: (1) to fund the continuing development of AEB1102; (2) to fund the advancement of any additional product candidates; and (3) to fund working capital, including general operating expenses. See Use of Proceeds.</p>
Directed share program	At our request, the underwriters have reserved up to 5% of the common stock being offered by this prospectus for sale at the initial public offering price to our directors, officers, employees and other individuals associated with us and members of their families. The sales will be made by UBS Financial Services Inc., a selected dealer affiliated with UBS Securities LLC, an underwriter of this offering, through a directed share program. We do not know if these persons will choose to purchase all or any portion of these reserved shares, but any purchases they do make will reduce the number of shares available to the general public. Any reserved shares not so purchased will be offered by the underwriters to the general public on the same terms as the other shares of common stock. Participants in the directed share program who purchase more than \$1,000,000 of shares shall be subject to a 25 day lock-up with respect to any shares sold to them pursuant to that program. This lock-up will have similar restrictions to the lock-up

agreements described in Underwriting Lock-Up Agreements. Any shares sold in the directed share program to our directors or executive officers shall be subject to the lock-up agreements described in

Underwriting Lock-Up Agreements. See Underwriting Directed Share Program. The underwriters will receive the same underwriting discount on any shares

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purchased by these parties as they will on any other shares sold to the public in this offering.

Insider Participation

Certain of our existing stockholders or their affiliates have agreed to purchase an aggregate of approximately 3,175,000 shares of our common stock in this offering at the initial public offering price. The underwriters will receive the same underwriting discount on the shares purchased by these parties as they will on the other shares sold to the public in this offering.

Risk factors

You should read the **Risk Factors** section of this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.

NASDAQ Global Market symbol

AGLE

The number of shares of our common stock to be outstanding after this offering is based on 7,929,832 shares, of our common stock outstanding as of December 31, 2015. This number is presented on a pro forma basis and gives effect to the automatic conversion of all outstanding shares of our convertible preferred stock into shares of common stock immediately prior to the completion of this offering, and excludes:

- n 629,848 shares of common stock issuable upon the exercise of options granted as of December 31, 2015, with a weighted-average exercise price of \$4.55 per share;
- n 84,417 shares of common stock issuable upon the exercise of options granted since January 1, 2016, with a weighted-average exercise price of \$5.46 per share; and
- n 1,859,286 shares of common stock reserved for future issuance under our stock-based compensation plans as of December 31, 2015, consisting of (a) 594,286 shares of common stock reserved for future issuance under our 2015 Equity Incentive Plan, (b) 1,100,000 shares of common stock reserved for future issuance under our 2016 Equity Incentive Plan, which became effective on the date immediately prior to the date of this prospectus and (c) 165,000 shares of common stock reserved for future issuance under our 2016 Employee Stock Purchase Plan, which became effective on the date of this prospectus. Upon completion of this offering, any remaining shares available for issuance under our 2015 Equity Incentive Plan will be added to the shares reserved under our 2016 Equity Incentive Plan and we will cease granting awards under our 2015 Equity Incentive Plan. Our 2016 Equity Incentive Plan also provides for automatic annual increases in the number of shares reserved under the plan each year, as more fully described in **Executive Compensation** **Employee Benefit and Stock Plans**.

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

- n the automatic conversion of all outstanding shares of our convertible preferred stock into shares of common stock immediately prior to the completion of this offering;
- n the effectiveness of our restated certificate of incorporation in connection with the completion of this offering;
- n a 10.5-to-1 reverse stock split of our capital stock that was effected on March 28, 2016;

- n no exercise of outstanding stock options;
- n no exercise of the underwriters' option to purchase additional shares of our common stock; and
- n no purchases by existing stockholders or their affiliates, described above or pursuant to the directed share program.

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The following table summarizes our consolidated statements of operations and balance sheet data. We have derived the summary consolidated statements of operations data for the years ended December 31, 2014 and 2015, and the summary consolidated balance sheet data as of December 31, 2015 from our audited consolidated financial statements appearing elsewhere in this prospectus. The summary statements of operations data presented below for the period from December 16, 2013 (inception) through December 31, 2013 are derived from our audited financial statements not included in this prospectus. Our historical results are not necessarily indicative of the results that may be expected in the future.

The summary consolidated financial data set forth below should be read together with the consolidated financial statements and related notes to those statements, as well as the sections of this prospectus captioned, Selected Consolidated Financial Data and Management's Discussion and Analysis of Financial Condition and Results of Operations.

	Period from December 16, 2013 (Inception) through December 31, 2013	Year Ended December 31, 2014	2015
	(in thousands, except share and per share amounts)		

Consolidated Statements of Operations Data:

Revenues:

Grant	\$		\$		\$	6,085
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Operating expenses:

Research and development	\$	1,150	\$	6,830	\$	11,453
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General and administrative		735		2,074		5,947
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Total operating expenses		1,885		8,904		17,400
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Loss from operations		(1,885)		(8,904)		(11,315)
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Other income (expense):

Interest income				1		22
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Change in fair value of forward sale contract		(52)		(1,444)		
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Other expense, net						(2)
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Total other income (expense):		(52)		(1,443)		20
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Net loss	\$	(1,937)	\$	(10,347)	\$	(11,295)
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Deemed dividend to convertible preferred stockholders						(228)
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Net loss allocable to common shareholders and stockholders	\$	(1,937)	\$	(10,347)	\$	(11,523)
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Common A-1 shares:

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Basic and diluted net loss per share	\$ (15.48)	\$ (20.13)	\$
Net loss attributable to class	\$ (1,277)	\$ (3,321)	\$
Basic and diluted weighted-average shares outstanding	82,500	165,000	
Common A shares:			
Basic and diluted net loss per share	\$ (3.94)	\$ (17.06)	\$
Net loss attributable to class	\$ (660)	\$ (5,706)	\$
Basic and diluted weighted-average shares outstanding	167,261	334,522	
Common B shares:			
Basic and diluted net loss per share	\$	\$ (40.17)	\$
Net loss attributable to class	\$	\$ (1,320)	\$
Basic and diluted weighted-average shares outstanding		32,861	
Common Stock:			
Basic and diluted net loss per share allocable to common stockholders	\$	\$	\$ (19.21)
Net loss allocable to common stockholders	\$	\$	\$ (11,523)
Basic and diluted weighted-average shares outstanding			599,788
Pro forma net loss per share (unaudited)(1)			
Basic and diluted net loss per share		\$	(1.69)
Basic and diluted weighted-average shares outstanding			6,820,042

(1) Refer to Note 12 of our consolidated financial statements for the year ended December 31, 2015 appearing elsewhere in the prospectus for a description of the method used to calculate unaudited pro forma basic and diluted net loss per share, unaudited supplemental pro forma basic and diluted net loss per share and weighted-average shares outstanding used to calculate the per share amounts.

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	As of December 31, 2015		
	Actual	Pro Forma(1)	Pro Forma, as Adjusted(2)
		(in thousands)	(unaudited)
Consolidated Balance Sheet Data:			
Cash, cash equivalents, and marketable securities	\$ 33,062	\$ 33,062	\$ 75,662
Working capital	35,763	35,763	78,363
Total assets	38,654	38,654	81,254
Total liabilities	2,550	2,550	2,550
Convertible preferred stock	58,311		
Accumulated deficit	(23,579)	(23,579)	(23,579)
Total stockholders (deficit) equity	(22,207)	36,104	78,704

- (1) Pro forma gives effect to the automatic conversion of all outstanding shares of our convertible preferred stock into shares of common stock upon the completion of this offering.
- (2) The pro forma as adjusted column reflects the pro forma adjustments described in footnote (1) above and the sale by us of 5,000,000 shares of common stock in this offering at the initial public offering price of \$10.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

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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 in this prospectus, including our consolidated financial statements and related notes, before investing in our common stock. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties that we are unaware of, or that we currently believe are not material, may also become important factors that affect us. If any of the following risks occur, our business, operating results and prospects could be materially harmed. In that event, the price of our common stock could decline, and you could lose part or all of your investment.

Risks Related to Our Business and Industry

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 are an early-stage biotechnology company. We began operations as a limited liability company in December 2013 and converted to a Delaware corporation in March 2015. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring and developing our technology, identifying potential product candidates, undertaking nonclinical studies, preparing to undertake clinical trials of our most advanced product candidate, and commencing clinical development in oncology for AEB1102.

We have not yet demonstrated our ability to successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain marketing 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. Products, on average, take ten to 15 years to be developed from the time they are discovered to the time they are approved and available for treating patients. Although we have recruited a team that has experience with clinical trials, as a company we have no experience in conducting clinical trials. In part because of this lack of experience, we cannot be certain that planned clinical trials will begin or be completed on time, if at all. Consequently, any predictions you make about our future success or viability based on our short operating history to date may not be as accurate as they could be if we had a longer operating history or an established track record in commercializing products or conducting clinical trials.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition from a company with a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We have no source of product revenue and we have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

We are an early-stage biotechnology company with a limited operating history. We have no approved products and have only recently begun clinical development of AEB1102 in oncology. Our ability to generate revenue and become profitable depends upon our ability to successfully complete the development of any of our product candidates, including AEB1102, for any of our target indications and to obtain necessary regulatory approvals. To date, we have recognized revenue solely from a government grant and have not generated any product revenue. Even if we receive regulatory approval for any of our product candidates, we do not know when these product candidates will generate revenue for us, if at all.

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In addition, since inception, we have incurred significant operating losses. Our net loss was \$11.3 million, \$10.3 million and \$1.9 million for the years ended December 31, 2015, December 31, 2014 and the period ended December 31, 2013, respectively. As of December 31, 2015, we had an accumulated deficit of \$23.6 million. We have financed our operations primarily through private placements of our preferred stock. We have devoted substantially all of our efforts to research and development. We have only very recently initiated clinical development for AEB1102 for oncology and have not initiated clinical development of our other product candidates and expect that it will be many years, if ever, before we have a product candidate ready for commercialization. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future, and the net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

- n continue our research, nonclinical and clinical development of our product candidates;
- n seek to identify additional product candidates;
- n conduct additional nonclinical studies and initiate clinical trials for our product candidates;
- n seek marketing approvals for any of our product candidates that successfully complete clinical trials, including pivotal trials;
- n ultimately establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval;
- n maintain, expand and protect our intellectual property portfolio;
- n hire additional executive, clinical, quality control and scientific personnel;
- n add operational, financial and management information systems and personnel, including personnel to support our product development; and
- n acquire or in-license other product candidates and technologies.

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 because of the numerous risks and uncertainties associated with product development. In addition, our expenses could increase significantly beyond expectations if we are required by the FDA, EMA, MHRA or other relevant regulatory authorities to perform studies in addition to those that we currently anticipate. Even if AEB1102, or any of our other product candidates, is approved for commercial sale, we anticipate incurring significant costs associated with the commercial launch of any product candidate.

To become and remain profitable, we must develop and eventually commercialize a product candidate or product candidates with significant market potential. This will require us to be successful in a range of challenging activities, including completing nonclinical testing, initiating and completing clinical trials of one or more of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those product candidates for which we obtain marketing approval and satisfying any post-marketing requirements. We may never succeed in these activities and, even if we do, we may never generate revenues that are significant or large enough to achieve profitability. We are currently only in the nonclinical development stages for most of our product candidates, and have only very recently initiated clinical development for AEB1102 for oncology. 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 would decrease the value of the company and could impair our ability to raise capital, maintain or expand our research and development efforts, expand our business or continue our operations. A decline in the value of our company would also cause you to lose part or even all of your investment.

We may not be successful in advancing the clinical development of our product candidates, including AEB1102.

In order to execute on our strategy of advancing the clinical development of our product candidates, we have designed our Phase 1 and Phase 2 trials of AEB1102 in the United States and

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Europe, respectively, for the treatment of Arginase I deficiency and our ongoing Phase 1 trial in the United States for the treatment of solid tumors. We have designed our planned Phase 1 trial of AEB1102 for the treatment of hematological malignancies and the expansion portion of our planned Phase 1 trial of AEB1102 for the treatment of tumors predicted to be dependent on arginine based on our biomarker studies in archival tumor samples and in patient-derived xenograft efficacy studies, or studies involving the growth of tissue or cells from one species in a different species. If our product candidate fails to work as we expect, our ability to assess the therapeutic effect, seek regulatory approval or otherwise begin or further clinical development, could be compromised. This may result in longer development times, larger trials and a greater likelihood of not obtaining regulatory approval.

In addition, as we pursue oncology-related applications of our product candidates, because the natural history of different tumor types is variable, we will need to study our product candidates, including AEB1102, in clinical trials specific for a given tumor type and this may result in increased time and cost. Even if our product candidate demonstrates efficacy in a particular tumor type, we cannot guarantee that any product candidate, including AEB1102, will behave similarly in all tumor types, and we will be required to obtain separate regulatory approvals for each tumor type we intend a product candidate to treat. If any of our planned clinical trials are unsuccessful, our business will suffer.

We or third parties may not be successful in developing companion diagnostic assays for our product candidates.

In developing a product candidate, we expect that if we use a biomarker-based test to identify and only enroll patients in clinical trials with tumors that express the biomarker, the FDA will require the development and regulatory approval of a companion diagnostic assay as a condition to approval of the product candidate. We do not have experience or capabilities in developing or commercializing these companion diagnostics and plan to rely in large part on third parties to perform these functions. Companion diagnostic assays are subject to regulation by the FDA as medical devices and require separate regulatory approval prior to the use of such diagnostic assays with a therapeutic product candidate. If we, or any third parties that we engage to assist us, are unable to successfully develop companion diagnostic assays for use with our product candidates, or experience delays in development, we may be unable to identify patients with the specific profile targeted by our product candidates for enrollment in our clinical trials. Accordingly, further investment may be required to further develop or obtain the required regulatory approval for the relevant companion diagnostic assay, which would delay or substantially impact our ability to conduct further clinical trials or obtain regulatory approval. In addition, if a companion diagnostic is necessary for any of our product candidates, the delay or failure to obtain regulatory approval of the companion diagnostic would delay or prevent the approval of the therapeutic product candidate. EMA, MHRA or comparable foreign regulatory authorities may also require the development and regulatory approval of a companion diagnostic assay as a condition to approval of the product candidate.

We will need substantial additional funding. If we are unable to raise capital when needed, we would be compelled to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our expenses to increase in parallel with our ongoing activities, particularly as we continue our discovery and nonclinical development to identify new clinical candidates and initiate clinical trials of, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our discovery and nonclinical development programs or any future clinical development or commercialization efforts.

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Based upon our planned use of the net proceeds, we estimate such funds will be sufficient for us to fund the planned Phase 1 trial in the United States, the planned Phase 2 trial in Europe for the treatment of patients with Arginase I deficiency, and to continue to fund our Phase 1 trial for AEB1102 for the treatment of solid tumors and initiate two other planned Phase 1 trials for AEB1102 for the treatment of cancer patients in the United States. Our future capital requirements will depend on many factors, including:

- n the costs associated with the scope, progress and results of compound discovery, nonclinical development, laboratory testing and clinical trials for our product candidates;
- n the costs related to the extent to which we enter into partnerships or other arrangements with third parties in order to further develop our product candidates;
- n the costs and fees associated with the discovery, acquisition or in-license of product candidates or technologies;
- n our ability to establish collaborations on favorable terms, if at all;
- n the costs of future commercialization activities, if any, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- n revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval; and
- n the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims.

Our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of product candidates that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives, which may not be available to us on acceptable terms, or at all.

Raising additional capital may cause dilution to our stockholders, including purchasers of common stock in this offering, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity or equity-linked offerings, debt financings, grants from research organizations and license and collaboration agreements. We do not have any committed external source of funds. 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 of these securities may rank senior to our common stock and include liquidation or other preferences, covenants or other terms that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us and/or that may reduce the value of our common stock.

We depend heavily on the success of our most advanced product candidate, AEB1102. All of our product candidates, other than AEB1102 in oncology, are still in nonclinical development or nonclinical testing, and for AEB1102 for oncology, the very early stages of clinical development. Future clinical trials of our product candidates may not be successful. If we are

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unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the nonclinical development and testing of our most advanced product candidate, AEB1102, for the treatment of Arginase I deficiency and cancer patients with solid tumors and hematological malignancies that are dependent on arginine. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of AEB1102. The success of AEB1102 and our other product candidates will depend on many factors, including the following:

- n successful enrollment of patients in, and the completion of, our planned clinical trials;
- n receiving marketing approvals from applicable regulatory authorities;
- n establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- n obtaining and maintaining patent and trade secret protection and non-patent exclusivity for our product candidates and their components;
- n enforcing and defending intellectual property rights and claims;
- n achieving desirable therapeutic properties for our product candidates intended indications;
- n launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with third parties;
- n acceptance of our product candidates, if and when approved, by patients, the medical community and third-party payors;
- n effectively competing with other therapies; and
- n maintaining an acceptable safety profile of our product candidates through clinical trials and following regulatory approval.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome. We may experience delays in completing, or ultimately be unable to complete, the development and commercialization of any of our product candidates.

We have only recently initiated a clinical trial of our lead product candidate AEB1102 in patients with solid tumors, and the risk of failure for all of our product candidates is high. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete nonclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans for the respective target indications. Clinical testing is expensive, difficult to design and implement and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process, and we have yet to commence any clinical trial for any of our product candidates, other than AEB1102 in oncology. Further, the results of nonclinical studies and future early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials that will likely differ in design and size from early-stage clinical trials, and interim results of a clinical trial do not necessarily predict final results. For example, for AEB1102 for oncology, we have only recently treated our first two cohorts of seven patients total, and while we have observed a temporary reduction in blood arginine, this data may not necessarily be predictive of the final results of all patients intended to be enrolled in this Phase 1 trial or in future trials. Moreover, nonclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in nonclinical studies and clinical trials have nonetheless failed to obtain marketing approval

of their products. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval.

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We may experience delays in our planned clinical trials and we do not know whether planned clinical trials will begin or enroll subjects on time, whether they will need to be redesigned or whether they will be able to be completed on schedule, if at all. There can be no assurance that the FDA, EMA, MHRA or any similar foreign regulatory agency will allow us to begin clinical trials or that they will not put any of the trials for any of our product candidates that enter clinical development on clinical hold in the future. We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates. Clinical trials may be delayed, suspended or prematurely terminated because costs are greater than we anticipate or for a variety of reasons, such as:

- n delay or failure in reaching agreement with the FDA, EMA, MHRA or a comparable foreign regulatory authority on a trial design that we are able to execute;
- n delay or failure in obtaining authorization to commence a trial or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a clinical trial;
- n delays in reaching, or failure to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with planned trial sites;
- n inability, delay, or failure in identifying and maintaining a sufficient number of trial sites, many of which may already be engaged in other clinical programs;
- n delay or failure in recruiting and enrolling suitable subjects to participate in one or more clinical trials;
- n delay or failure in having subjects complete a trial or return for post-treatment follow-up;
- n clinical sites and investigators deviating from the trial protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial;
- n a clinical hold for any of our planned clinical trials, including for AEB1102, where a clinical hold in a trial in one indication would result in a clinical hold for clinical trials in other indications;
- n clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct more clinical trials than we anticipate or abandon product development programs;
- n the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or insufficient or participants may drop out of these clinical trials at a higher rate than we anticipate;
- n we may experience delays or difficulties in the enrollment of patients with Arginase I deficiency or cancer patients with tumors or hematological malignancies dependent on arginine, including the identification of patients with Arginase I deficiency or development or identification of a test, if needed, to screen for those cancer patients;
- n our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- n we may have difficulty partnering with experienced CROs that can screen for cancer patients with tumors or hematological malignancies dependent on arginine that AEB1102 is designed to target and with CROs that can run our clinical trials effectively;
- n regulators may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- n the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; or
- n there may be changes in governmental regulations or administrative actions.

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If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully initiate or complete clinical trials of our product candidates or other testing, if the results of these trials or tests do not demonstrate sufficient clinical benefit or if our product candidates do not have an acceptable safety profile, we may:

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

We do not know whether any of our planned or current nonclinical studies or planned clinical trials will need to be restructured or will be completed on schedule, or at all. For example, we withdrew our initial IND for the treatment of Arginase I deficiency in order to comply with new draft guidance issued by the FDA that required additional toxicology studies. In addition, we originally proposed including subjects younger than age 18 in our initial Phase 1 trial in patients with Arginase I deficiency; however, the FDA stated that enrollment in this Phase 1 trial must currently be limited to adult patients 18 years and older. Significant nonclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may materially harm our business and results of operations.

We may not be able to submit INDs, or foreign equivalents outside of the United States, to commence clinical trials for product candidates on the timeframes we expect, and even if we are able to, the FDA, EMA, MHRA or comparable foreign regulatory authorities may not permit us to proceed with planned clinical trials.

We are currently conducting nonclinical development of our product candidates other than our clinical trial for AEB1102 for the treatment of solid tumors. Progression of any candidate into clinical trials is inherently risky and dependent on the results obtained in nonclinical programs, and other potential results such as the results of other clinical programs and results of third-party programs. If results are not available when expected or problems are identified during therapy development, we may experience significant delays in clinical development. This may also impact our ability to achieve certain financial milestones and the expected timeframes to market any of our product candidates. Failure to submit or have effective INDs, CTAs or other comparable foreign equivalents and commence clinical programs will significantly limit our opportunity to generate revenue.

Our engineered human enzyme product candidates for our oncology indications represent a novel approach to cancer treatment, which could result in heightened regulatory scrutiny, delays in clinical development, or delays in our ability to achieve regulatory approval or commercialization of our product candidates.

Engineered human enzyme products are a new category of therapeutics. Because this is a relatively new and expanding area of novel therapeutic interventions, there can be no assurance as to the length of the trial period, the number of patients the FDA, EMA, MHRA or another applicable regulatory authority will require to be enrolled in the trials in order to establish the safety, efficacy, purity and potency of engineered human enzyme products, or that the data generated in these trials will be acceptable to the FDA or another applicable regulatory authority to support marketing approval.

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We have only very recently initiated enrollment in our Phase 1 clinical trial for the treatment of solid tumors for AEB1102 and treated our first two cohorts of seven patients total. We have not dosed any of our other product candidates in humans. Our planned clinical trials may reveal significant adverse events, toxicities or other side effects not seen in our nonclinical studies and may result in a safety profile that could inhibit regulatory approval or market acceptance of any of our product candidates.

In order to obtain marketing approval for any of our product candidates, we must demonstrate the safety and efficacy of the product candidate for the relevant clinical indication or indications through nonclinical studies and clinical trials as well as additional supporting data. If our product candidates are associated with undesirable side effects in nonclinical studies or clinical trials or have characteristics that are unexpected, we may need to interrupt, delay or abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective.

We have only very recently initiated enrollment for our clinical trial for AEB1102 for the treatment of solid tumors and treated our first two cohorts of seven patients total. Given the nature of the patient population enrolled in this trial, we expect to and have observed serious adverse events in some of these patients, including death. Six serious adverse events were reported in a total of four patients. These included hypercalcemia, bacteremia, pericardial effusion, respiratory failure and worsening of the patients' underlying cancer, none of which were assessed as trial therapy-related. All patients recovered except for one who died after discontinuing the trial due to worsening of the underlying cancer. To date, we do not consider any of these serious adverse events to be drug-related and are proceeding with the dosing schedule. We have not dosed any of our other product candidates in humans. Subjects in our ongoing and planned clinical trials may suffer significant serious adverse events, including those that are drug-related, or other side effects not observed in our nonclinical studies, including, but not limited to, immune responses, organ toxicities such as liver, heart or kidney or other tolerability issues.

Testing in animals, such as our primate studies in AEB1102, may not uncover all side effects in humans or any observed side effects in animals may be more severe in humans. For example, it is possible that patients' immune systems may recognize our engineered human enzymes as foreign and trigger an immune response. This risk is heightened in patients who lack the target enzyme, as is the case with patients with Arginase I deficiency we will be treating in our planned Phase 1 dose escalation and Phase 2 trials for this IEM. In addition, our product candidates such as AEB1102 break down target amino acids such as arginine, thereby releasing metabolites such as ornithine into the bloodstream. Some patients may be sensitive to these metabolites, increasing the risk of an adverse reaction due to treatment, which risk may not be able to be mitigated through dosing. Finally, although our engineered human enzyme product candidates such as AEB1102 are engineered from the human genome, AEB1102 is produced in *E. coli*. This manufacturing process could lead AEB1102 to be more likely to trigger an immune response than we expect.

To the extent significant adverse events or other side effects are observed in any of our clinical trials, we may have difficulty recruiting patients to the clinical trial, patients may drop out of our trial, or we may be required to abandon the trial or our development efforts of that product candidate altogether. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early-stage studies have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the drug from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance of the approved product due to its tolerability versus other therapies. Any of these developments could materially harm our business, financial condition and prospects.

Further, toxicities associated with our product candidates may also develop after regulatory approval and lead to the withdrawal of the product from the market. We cannot predict whether our

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product candidates will cause organ or other injury in humans that would preclude or lead to the revocation of regulatory approval based on nonclinical studies or early stage clinical testing.

If we experience delays or difficulties in the enrollment of patients in our planned clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue our planned clinical trials if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA, EMA, MHRA or comparable regulatory authorities outside the United States. More specifically, many of our product candidates, including AEB1102, initially target indications that may be characterized as orphan markets, which can prolong the clinical trial timeline for the regulatory process if sufficient patients cannot be enrolled in a timely manner. Arginase I deficiency, for example, is the least common of the urea cycle disorders, with a reported incidence of 1:350,000 to 1:1,000,000 live births. Urea cycle disorders are the IEM found in the enzymes of the urea cycle, the process by which the human body detoxifies ammonia, a natural byproduct of protein metabolism. We believe that approximately 500-600 individuals in the United States and Europe suffer from Arginase I deficiency. While there is currently a neonatal blood test to screen for Arginase I deficiency, it has only been in broad use in the United States since 2006 and is not commonly used in Europe. We plan initially to treat patients who are 18 and older in the United States and 12 and older in Europe, and many in these age categories have not been screened for Arginase I deficiency, which may make it more difficult to enroll patients in our initial clinical trials for this indication. One urea cycle disorder physician consortium and one urea cycle disorder patient group have together identified an aggregate of approximately 20 patients with Arginase I deficiency in the United States and approximately 16 in Europe. Because neonatal blood testing for this disorder did not become common in the United States until 2006, we believe that approximately half of those identified in the United States are younger than 18, and thus would not be eligible for inclusion in our proposed Phase 1 trial in the United States.

Our planned toxicology program includes conducting six months of juvenile rat studies prior to the initiation of the Phase 2 trial in Europe. Based on our discussions with the MHRA, we believe these data will support the treatment of patients two years of age and older in Europe. We have substantially completed a toxicology study in the United States that we believe will support the dosing of patients two years of age and older in the United States in future clinical trials. However, we cannot guarantee that we will be able to enroll sufficient patients in our clinical trials or that the MHRA or FDA will permit us to enroll additional patient populations in the future based on these nonclinical studies.

Delays in patient enrollment could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our technology or termination of the clinical trials altogether.

Patient enrollment is affected by factors including:

- n the severity of the disease under investigation;
- n the design of the clinical trial protocol;
- n the novelty of the product candidate and acceptance by physicians;
- n the patient eligibility criteria for the study in question;
- n the size of the total patient population;
- n the design of the clinical trials;
- n the perceived risks and benefits of the product candidate under study;
- n our payments for conducting clinical trials;

- n the patient referral practices of physicians;
- n the ability to monitor patients adequately during and after treatment with the product candidate; and
- n the proximity and availability of clinical trial sites for prospective patients.

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In addition, some patients with Arginase I deficiency suffer from heightened levels of ammonia, or hyperammonemia. Hyperion Therapeutics, Inc., which has been acquired by Horizon Pharma plc, has gained approval for its product RAVICTI (glycerol phenylbutyrate) to treat patients with urea cycle disorders suffering from hyperammonemia. Some patients who may be eligible for our planned clinical trials may instead pursue treatment for this effect of their condition by taking RAVICTI (glycerol phenylbutyrate) or through dietary protein restriction. Our inability to enroll a sufficient number of patients for any of our clinical trials could result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates and in delays to commercially launching our product candidates, if approved, which would cause the value of our company to decline and limit our ability to obtain additional financing.

Even though we have obtained orphan drug designation for AEB1102, we may not obtain or maintain orphan drug exclusivity for AEB1102 or we may not obtain orphan drug designation or exclusivity for any of our other product candidates.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs or biologics for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same drug for that time period. The applicable period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

On March 16, 2015, we obtained orphan drug designation in the United States for AEB1102 for the treatment of patients with hyperargininemia, also known as Arginase I deficiency. A company that first obtains FDA approval for a designated orphan drug for the specified rare disease or condition receives orphan drug marketing exclusivity for that drug for a period of seven years. This orphan drug exclusivity prevents the FDA from approving another application, including a Biologics License Application, or BLA, to market a drug containing the same active moiety, or principal molecular structure, for the same orphan indication, except in very limited circumstances, including when the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation.

Even though we have received orphan drug designation for AEB1102 for the treatment of Arginase I deficiency, we may not be the first to obtain marketing approval for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical product candidates. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition or a drug with the same active moiety can be approved for a different indication. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. In addition, even if we intend to seek orphan drug designation for other product candidates, we may never receive such designations or obtain orphan drug exclusivity.

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If the market opportunities for our product candidates are smaller than we believe they are, our future product revenues may be adversely affected and our business may suffer.

Our understanding of both the number of people who suffer from conditions such as Arginase I deficiency or who have tumors or hematological malignancies dependent on arginine, as well as the potential subset of those who have the potential to benefit from treatment with our product candidates such as AEB1102, are based on estimates. These estimates may prove to be incorrect and new studies may reduce the estimated incidence or prevalence of these diseases. The number of patients in the United States, Europe or elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our product candidates or patients may become increasingly difficult to identify and access, all of which would adversely affect our business, financial condition, results of operations and prospects.

Further, there are several factors that could contribute to making the actual number of patients who receive our potential product candidates less than the potentially addressable market. These include the lack of widespread availability of, and limited reimbursement for, new therapies in many underdeveloped markets.

Even if any of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success. For example, current cancer treatments like chemotherapy and radiation therapy are well established in the medical community, and physicians may continue to rely on these treatments instead of adopting the use of AEB1102 for the treatment of patients with arginine dependent cancers. In addition, many new drugs have been recently approved and many more are in the pipeline to treat patients with cancer. Additionally, current treatments for Arginase I deficiency include dietary protein restriction and, in some instances, ammonia-scavenging drugs such as RAVICTI (glycerol phenylbutyrate). If our product candidates do not achieve an adequate level of acceptance, we may never generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- n their efficacy, safety and other potential advantages compared to alternative treatments;
- n our ability to offer them for sale at competitive prices;
- n their convenience and ease of administration compared to alternative treatments;
- n the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- n the strength of marketing and distribution support;
- n the availability of third-party coverage and adequate reimbursement for our product candidates;
- n the prevalence and severity of their side effects;
- n any restrictions on the use of our product candidates together with other medications;
- n interactions of our product candidates with other products patients are taking; and
- n inability of patients with certain medical histories to take our product candidates.

We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and, as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of product candidate development, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution.

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We currently do not have a marketing or sales team for the marketing, sales and distribution of any of our product candidates that are able to obtain regulatory approval. In order to commercialize any product candidates, we must build on a territory-by-territory basis marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. If our product candidates receive regulatory approval, we intend to establish an internal sales or marketing team with technical expertise and supporting distribution capabilities to commercialize our product candidates, which will be expensive and time consuming and will require significant attention of our executive officers to manage. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of any of our product candidates that we obtain approval to market. With respect to the commercialization of all or certain of our product candidates, we may choose to collaborate, either globally or on a territory-by-territory basis, with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. If we are unable to enter into such arrangements when needed on acceptable terms, or at all, we may not be able to successfully commercialize any of our product candidates that receive regulatory approval or any such commercialization may experience delays or limitations. If we are not successful in commercializing our product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we may incur significant additional losses.

To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

We face significant competition from other biotechnology and pharmaceutical companies and our operating results will suffer if we fail to compete effectively.

The biotechnology and pharmaceutical industries are intensely competitive. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, biotechnology companies, universities and other research institutions. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations and well-established sales forces. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing, on an exclusive basis, product candidates that are more effective or less costly than any product candidate that we are currently developing or that we may develop.

We face intense competition from companies developing products to address urea cycle disorders. For example, Hyperion Therapeutics, Inc., which has been acquired by Horizon Pharma plc, has gained approval for its drug RAVICTI (glycerol phenylbutyrate), which is used to treat patients with urea cycle disorders suffering from hyperammonemia, which may sometimes include patients suffering from Arginase I deficiency. Patients with Arginase I deficiency may also benefit from taking RAVICTI (glycerol phenylbutyrate). We also face intense competition from companies developing products and therapies to treat cancer. For example, Polaris Pharmaceuticals is conducting numerous clinical trials of ADI-PEG 20, an enzyme derived from mycoplasma, which degrades arginine in the blood.

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Our ability to compete successfully will depend largely on our ability to leverage our experience in product candidate discovery and development to:

- n discover and develop product candidates that are superior to other products in the market;
- n attract qualified scientific, product development and commercial personnel;
- n obtain and maintain patent and/or other proprietary protection for our product candidates and technologies;
- n obtain required regulatory approvals; and
- n successfully collaborate with research institutions or pharmaceutical companies in the discovery, development and commercialization of new product candidates.

The availability and price of our competitors' products could limit the demand, and the price we are able to charge, for any of our product candidates, if approved. We will not achieve our business plan if acceptance is inhibited by price competition or the reluctance of physicians to switch from existing drug products or other therapies to our product candidates, or if physicians switch to other new drug products or choose to reserve our product candidates for use in limited circumstances.

Established biotechnology companies may invest heavily to accelerate discovery and development of products that could make our product candidates less competitive. 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. Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA or non-U.S. regulatory approval or discovering, developing and commercializing product candidates before we do, which would have a material adverse impact on our business. Many of our competitors have greater resources than we do and have established sales and marketing capabilities, whether internally or through third parties. We will not be able to successfully commercialize our product candidates without establishing sales and marketing capabilities internally or through strategic partners.

The insurance coverage and reimbursement status of newly-approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for new or current product candidates could limit our ability to market those product candidates and decrease our ability to generate revenue.

The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford expensive treatments. Sales of any of our product candidates that receive marketing approval will depend substantially, both in the United States and internationally, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about reimbursement for new products are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services since CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for novel products such as ours since there is no body of established practices and precedents for these new products. Reimbursement agencies in Europe may be more conservative than CMS. For example, a number of

cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in certain European countries.

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Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada and other countries has and will continue to put pressure on the pricing and usage of therapeutics such as our product candidates. In many countries, particularly the countries of the European Union, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In general, the prices of products under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

Moreover, increasing efforts by governmental and third-party payors, in the United States and internationally, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products into the healthcare market.

In addition to CMS and private payors, professional organizations such as the National Comprehensive Cancer Network and the American Society of Clinical Oncology can influence decisions about reimbursement for new products by determining standards for care. In addition, many private payors contract with commercial vendors who sell software that provide guidelines that attempt to limit utilization of, and therefore reimbursement for, certain products deemed to provide limited benefit to existing alternatives. Such organizations may set guidelines that limit reimbursement or utilization of our product candidates.

Furthermore, some of our target indications, including for Arginase I deficiency for AEB1102, are orphan indications where patient populations are small. In order for therapeutics that are designed to treat smaller patient populations to be commercially viable, the reimbursement for such therapeutics must be higher, on a relative basis, to account for the lack of volume. Accordingly, we will need to implement a coverage and reimbursement strategy for any approved product candidate that accounts for the smaller potential market size. If we are unable to establish or sustain coverage and adequate reimbursement for any future product candidates from third-party payors, the adoption of those products and sales revenue will be adversely affected, which, in turn, could adversely affect the ability to market or sell those product candidates, if approved.

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are an early-stage nonclinical development company with a limited operating history, and, as of February 29, 2016, had only 23 employees, including four executive officers. We are highly dependent on the research and development, clinical and business development expertise of Dr. David G. Lowe, our President and Chief Executive Officer, as well as the other principal members of our management, scientific and clinical team. Any of our management team members may terminate their employment with us at any time. We do not maintain key person insurance for any of our executives or other employees.

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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, facilitate regulatory approval of and commercialize product candidates. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. 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 discovery and nonclinical 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 product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.

With the enactment of the Biologics Price Competition and Innovation Act of 2009, or BPCIA, an abbreviated pathway for the approval of biosimilar and interchangeable biological products was created. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as interchangeable based on its similarity to an existing reference product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product is approved under a BLA. On March 6, 2015, the FDA approved the first biosimilar product under the BPCIA. However, the law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when the processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

We believe that if any of our product candidates are approved as a biological product under a BLA, it should qualify for the 12-year period of exclusivity. However, there is a risk that the FDA will not consider any of our product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Additionally, this period of regulatory exclusivity does not apply to companies pursuing regulatory approval via their own traditional BLA, rather than via the abbreviated pathway. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products that may be approved in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

Our business and operations would suffer in the event of system failures.

Despite the implementation of security measures, our internal computer systems and those of our strategic partners and third-parties on whom we rely are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Furthermore, we have little or no control over the security measures and computer systems of third parties including the University of Texas at Austin and any CROs we may work with in the future. While we and, to our knowledge, our third-party strategic partners have not experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, or the operations of our strategic partner KBI BioPharma, Inc., or KBI, the University

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Texas at Austin or our other third-party strategic partners, it could result in a material disruption of our product candidate development programs. For example, the loss of research data by University of Texas at Austin could delay development of our product candidates and the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts, and we may incur substantial costs to attempt to recover or reproduce the data. If any disruption or security breach resulted in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability or the further development of our product candidates could be delayed.

Risks Related to Our Reliance on Third Parties

We will rely on third parties to conduct our planned clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We currently rely and will continue to rely on third parties to provide manufacturing, discovery and clinical development capabilities. For example, we rely on the University of Texas at Austin to provide research under our sponsored research agreement, and we rely on our strategic partner KBI to manufacture and supply nonclinical and clinical trial quantities of the biological substance of our lead product candidate, AEB1102. Until we develop our own drug discovery capabilities, we will continue to depend on third parties such as the University of Texas at Austin for the identification of future targets for our product candidates.

We will rely on third-party CROs to conduct our planned clinical trials of AEB1102. We do not plan to independently conduct clinical trials of our other product candidates. These agreements might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, that would delay our product development activities.

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, we will remain responsible for ensuring that each of our planned clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with regulatory standards, commonly referred to as good clinical practices for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Other countries regulatory agencies also have requirements for clinical trials with which we must comply. We also will be required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, *ClinicalTrials.gov*, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our planned clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to complete our clinical trials, obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

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 product candidates, producing additional losses and depriving us of potential product revenue.

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We contract with third parties for the manufacture of our product candidates for nonclinical and planned clinical testing and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates at an acceptable cost and quality, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate facilities for the manufacture of our product candidates, and we do not have any manufacturing personnel. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. We rely, and expect to continue to rely, on third parties, including KBI and Lyophilization Services of New England, Inc., for the manufacture of our product candidates for nonclinical and for our future planned clinical testing. We will rely on third parties as well for commercial manufacture if any of our product candidates receive marketing approval. 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 performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a source for bulk drug substance. Currently, KBI is expected to supply the drug substance requirements for our planned clinical trials with AEB1102. If KBI cannot supply us with sufficient amounts, pursuant to product requirements as agreed, we may be required to identify alternative manufacturers, which would lead us to incur added costs and delays in identifying and qualifying any replacement.

The formulation used in early studies is not a final formulation for commercialization. If we are unable to demonstrate that our commercial scale product is comparable to the product used in clinical trials, we may not receive regulatory approval for that product without additional clinical trials. We cannot guarantee that we will be able to make the required modifications within currently anticipated timeframes or that such modifications, if and when made, will obtain regulatory approval or that the new processes or modified processes will successfully be transferred to the third-party contract suppliers within currently anticipated timeframes. These may require additional studies, and may delay our clinical trials and/or commercialization.

We expect to rely on third-party manufacturers or third-party strategic partners for the manufacture of commercial supply of any other product candidates for which our strategic partners or we obtain marketing approval. The process of manufacturing and administering our product candidates is complex and highly regulated. As a result of the complexities, our manufacturing and supply costs are likely to be higher than those at more traditional manufacturing processes and the manufacturing process is less reliable and more difficult to reproduce.

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 product candidates, producing additional losses and depriving us of potential product revenue.

We may be unable to establish any additional agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers on acceptable terms, reliance on third-party manufacturers entails additional risks, including:

- n possible noncompliance by the third party with regulatory requirements and quality assurance;
- n the possible breach of the manufacturing agreement by the third party;

n the possible misappropriation of our proprietary information, including our trade secrets and know-how; and

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- n the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with current good manufacturing practices, or cGMP or similar regulatory requirements outside the United States. Although we do not have day-to-day control over third-party manufacturers' compliance with these regulations and standards, we are responsible for ensuring compliance with such regulations and standards. 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, operating restrictions and criminal prosecutions, any of which would significantly and adversely affect supplies of our product candidates and our business.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. 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 may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

Failure of any future third-party collaborators to successfully commercialize companion diagnostics developed for use with our therapeutic product candidates for oncology indications could harm our ability to commercialize these product candidates.

We do not plan to develop companion diagnostics internally and, as a result, we are dependent on the efforts of our third-party strategic partners to successfully commercialize any needed companion diagnostics. Our strategic partners:

- n may not perform their obligations as expected;
- n may encounter production difficulties that could constrain the supply of the companion diagnostics;
- n may have difficulties gaining acceptance of the use of the companion diagnostics in the clinical community;
- n may not pursue commercialization of any companion diagnostics;
- n may elect not to continue or renew commercialization programs based on changes in the strategic partners' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- n may not commit sufficient resources to the marketing and distribution of such companion diagnostic product candidates; and
- n may terminate their relationship with us.

If companion diagnostics needed for use with our therapeutic product candidates in oncology fail to gain market acceptance, our ability to derive revenues from sales of these therapeutic product candidates could be harmed. If our strategic partners fail to commercialize these companion diagnostics, it could adversely affect and delay the development or commercialization of our therapeutic product candidates.

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We may not be successful in finding strategic partners for continuing development of certain of our product candidates or successfully commercializing or competing in the market for certain indications.

We may seek to develop strategic partnerships for developing certain of our product candidates, due to capital costs required to develop the product candidates or manufacturing constraints. We may not be successful in our efforts to establish such a strategic partnership or other alternative arrangements for our product candidates because our research and development pipeline may be insufficient, our product candidates may be deemed to be at too early of a stage of development for collaborative effort or third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy. In addition, we may be restricted under existing collaboration agreements from entering into future agreements with potential strategic partners. We cannot be certain that, following a strategic transaction or license, we will achieve an economic benefit that justifies such transaction.

If we are unable to reach agreements with suitable strategic partners on a timely basis, on acceptable terms or at all, we may have to curtail the development of a product candidate, reduce or delay its development program, delay its potential commercialization, reduce the scope of any sales or marketing activities or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates and our business, financial condition, results of operations and prospects may be materially and adversely affected.

Our employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable non-U.S. regulatory authorities, provide accurate information to the FDA or comparable non-U.S. regulatory authorities, comply with manufacturing standards we have established, comply with the Foreign Corrupt Practices Act and federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, 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, standards or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these employees or we have used or disclosed intellectual

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property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

We and our strategic partners that we rely on may be adversely affected by natural disasters, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters could severely disrupt our operations or the operations of KBI's manufacturing facilities and have a material adverse effect on our business, financial condition, results of operations and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as KBI's manufacturing facilities, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and may not prove adequate in the event of a serious disaster or similar event. KBI's manufacturing facility, as well as substantially all of our current supply of product candidates is located in Durham, North Carolina, and we do not have any existing back-up facilities in place or plans for such back-up facilities. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Government Regulation

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals in the United States or in foreign jurisdictions, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates must be approved by the FDA pursuant to a BLA in the United States, and by the EMA pursuant to a MAA, and by other comparable regulatory authorities outside the United States prior to commercialization. The process of obtaining marketing approvals, both in the United States and internationally, is expensive and takes many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval in Europe or another non-U.S. jurisdiction may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or our third-party strategic partners may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other

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countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our product candidates in any market.

Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have no experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party CROs to assist us in this process. Securing marketing approval requires the submission of extensive nonclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional nonclinical, clinical or other studies. In addition, varying interpretations of the data obtained from nonclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may also cause delays in or prevent the approval of an application.

Approval of our product candidates may be delayed or refused for many reasons, including the following:

- n the FDA, EMA, MHRA or other comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- n we may be unable to demonstrate to the satisfaction of the FDA, EMA, MHRA or other comparable foreign regulatory authorities that our product candidates are safe and effective for any of their proposed indications;
- n the results of clinical trials may not meet the level of statistical significance required by the FDA, EMA, MHRA or other comparable foreign regulatory authorities for approval;
- n we may be unable to demonstrate that our product candidates' clinical and other benefits outweigh their safety risks;
- n the FDA, EMA, MHRA or other comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical programs or clinical trials;
- n the data collected from clinical trials of our product candidates may not be sufficient to the satisfaction of the FDA, EMA, MHRA or other comparable foreign regulatory authorities to support the submission of a BLA, MAA or other comparable submission in other jurisdictions or to obtain regulatory approval in the United States or elsewhere;
- n the facilities of the third-party manufacturers with which we partner may not be adequate to support approval of our product candidates; and
- n the approval policies or regulations of the FDA, EMA or other comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

New products for the treatment of cancer frequently are initially indicated only for patient populations that have not responded to an existing therapy or have relapsed. If any of our product candidates receives marketing approval, the approved labeling may limit the use of our product candidates in this way, which could limit sales of the product.

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Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable. If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

A Fast Track Designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.

We do not currently have Fast Track Designation for any of our product candidates but intend to seek such designation for some or all of our product candidates. If a drug or biologic is intended for the treatment of a serious or life-threatening condition and the drug or biologic demonstrates the potential to address unmet medical needs for this condition, the drug or biologic sponsor may apply for FDA Fast Track Designation. The FDA has broad discretion whether or not to grant this designation. Even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Many drugs or biologics that have received Fast Track Designation have failed to obtain approval.

We may also seek accelerated approval for products that have obtained fast track designation. Under the FDA's accelerated approval program, the FDA may approve a drug or biologic for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. For drugs or biologics granted accelerated approval, post-marketing confirmatory trials are required to describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. These confirmatory trials must be completed with due diligence and, in some cases, the FDA may require that the trial be designed and/or initiated prior to approval. Moreover, the FDA may withdraw approval of our product candidate or indication approved under the accelerated approval pathway if, for example:

- n the trial or trials required to verify the predicted clinical benefit of our product candidate fail to verify such benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the drug;
- n other evidence demonstrates that our product candidate is not shown to be safe or effective under the conditions of use;
- n we fail to conduct any required post-approval trial of our product candidate with due diligence; or
- n we disseminate false or misleading promotional materials relating to the relevant product candidate.

A Breakthrough Therapy Designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.

We do not currently have Breakthrough Therapy Designation for any of our product candidates, but may seek such designation. A Breakthrough Therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug or biologic may demonstrate

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substantial improvement over existing therapies with respect to one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs or biologics that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor can help to identify the most efficient path for development.

Designation as a Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe, after completing early clinical trials, that one of our product candidates meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy designation for a product candidate may not result in a faster development process, review or approval compared to drugs or biologics considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as Breakthrough Therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification.

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

Our product candidates and the activities associated with their development and commercialization, including their testing, manufacture, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, including periodic inspections by the FDA and other regulatory authorities, requirements regarding the distribution of samples to physicians and recordkeeping.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of any approved product. The FDA closely regulates the post-approval marketing and promotion of drugs and biologics to ensure drugs and biologics are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers communications regarding use of their products and if we promote our product candidates beyond their approved indications, we may be subject to enforcement action for off-label promotion. Violations of the Federal Food, Drug, and Cosmetic Act relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our product candidates, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- n restrictions on such product candidates, manufacturers or manufacturing processes;
- n restrictions on the labeling or marketing of a product;
- n restrictions on product distribution or use;
- n requirements to conduct post-marketing studies or clinical trials;
- n warning or untitled letters;
- n withdrawal of any approved product from the market;

- n refusal to approve pending applications or supplements to approved applications that we submit;
- n recall of product candidates;
- n fines, restitution or disgorgement of profits or revenues;

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- n suspension or withdrawal of marketing approvals;
- n refusal to permit the import or export of our product candidates;
- n product seizure; or
- n injunctions or the imposition of civil or criminal penalties.

Non-compliance with European requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with Europe's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any product candidates for which we obtain marketing approval. Restrictions under applicable U.S. federal and state healthcare laws and regulations include the following:

- n the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- n the federal False Claims Act imposes criminal and civil penalties, including civil whistleblower or *qui tam* actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- n the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- n HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- n federal law requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals, which includes annual data collection and reporting obligations. The information was made publicly available on a searchable website in September 2014 and will be disclosed on an annual basis; and
- n analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information

in some circumstances, many of

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which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of product candidates from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or 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. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved product candidates. While the MMA only applies to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

More recently, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

Among the provisions of the ACA of importance to our potential product candidates are the following:

- n an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- n an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- n expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;

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- n a Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;
- n extension of manufacturers' Medicaid rebate liability to manage care initiation;
- n expansion of eligibility criteria for Medicaid programs;
- n expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- n requirements to report financial arrangements with physicians and teaching hospitals;
- n a requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- n a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

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 that we believe is consistent with industry norms to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, we cannot assure you that it will be sufficient to cover our liability in such cases. We do not maintain insurance for environmental liability or toxic tort claims that may be

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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 discovery, nonclinical development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain intellectual property protection for our technology and product candidates, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and product candidates similar or identical to ours, and our ability to successfully commercialize our technology and product candidates may be impaired.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and product candidates, including any companion diagnostic developed by us or a third-party strategic partner. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and product candidates. Our patent portfolio includes patents and patent applications we exclusively licensed or that were assigned to us by the University of Texas at Austin. This patent portfolio includes issued patents and pending patent applications covering compositions of matter and methods of use.

The patent prosecution process is expensive and time-consuming, and we may not be able to file, prosecute, maintain, enforce or license all necessary or desirable patent applications at a reasonable cost or in a timely manner, or in all jurisdictions. We may choose not to seek patent protection for certain innovations and may choose not to pursue patent protection in certain jurisdictions, and under the laws of certain jurisdictions, patents or other intellectual property rights may be unavailable or limited in scope. It is also possible that we will fail to identify patentable aspects of our discovery and nonclinical development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. We may also require the cooperation of our licensors in order to enforce the licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. The U.S. Patent and Trademark Office, or U.S. PTO, has not established a consistent policy regarding the breadth of claims that it will allow in biotechnology patents. In addition, the laws of foreign jurisdictions may not protect our rights to the same extent as the laws of the United States. For example, India and China do not allow patents for methods of treating the human body. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions, nor can we know whether those from whom we license patents were the first to make the inventions claimed or were the first to file. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our technology or product candidates, in whole or in part, or which effectively prevent others from

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commercializing competitive technologies and product candidates. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The U.S. PTO recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition. Depending on future actions by the U.S. Congress, the federal courts, and the U.S. PTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. In addition, there may be patent law reforms in foreign jurisdictions that could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents in those foreign jurisdictions.

Moreover, we may be subject to a third-party preissuance submission of prior art to the U.S. PTO or patent offices in foreign jurisdictions, or become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize product candidates without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or product candidates in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and product candidates, or limit the duration of the patent protection of our technology and product candidates. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours.

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The risks pertaining to our patents and other intellectual property rights also apply to the intellectual property rights that we license, and any failure to obtain, maintain and enforce these rights could have a material adverse effect on our business. In some cases we may not have control over the prosecution, maintenance or enforcement of the patents that we license, and our licensors may fail to take the steps that we believe are necessary or desirable in order to obtain, maintain and enforce the licensed patents. Any inability on our part to protect adequately our intellectual property may have a material adverse effect on our business, operating results and financial position.

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, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the U.S. PTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay these fees due to non-U.S. patent agencies. The U.S. PTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates and technology, including interference or derivation proceedings before the U.S. PTO and similar bodies in other jurisdictions. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our product candidates and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

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Any lawsuits relating to infringement of intellectual property rights necessary to defend ourselves or enforce our rights will be costly and time consuming, and could be unsuccessful.

Because competition in our industry is intense, competitors may infringe or otherwise violate our issued patents, patents of our licensors or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming, and could distract our technical and management personnel from their normal responsibilities. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or 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 proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. We may also elect to enter into license agreements in order to settle patent infringement claims or to resolve disputes prior to litigation, and any such license agreements may require us to pay royalties and other fees that could be significant. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure.

We may not be successful in obtaining or maintaining necessary rights for our development pipeline through acquisitions and in-licenses.

Presently we have rights to intellectual property to develop our product candidates, including patents and patent applications we exclusively licensed from, or were assigned to us by, the University of Texas at Austin or one of our founders. Because our programs may involve additional product candidates that may require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license or use these proprietary rights. We currently plan on licensing rights to targets for our product candidates since we are in the process of attempting to develop our own internal drug discovery capabilities. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to required third-party intellectual property rights, our business, financial condition and prospects for growth could suffer.

We partner with the University of Texas at Austin, which is a U.S. academic institution, in order to accelerate our discovery and nonclinical development work under a Sponsored Research Agreement. Under the Sponsored Research Agreement, we made payments of \$386,000 and \$563,000 for the years ended December 31, 2014 and 2015, respectively, to sponsor research in the laboratory of our director Dr. George Georgiou at the University of Texas at Austin on the engineering, optimization and initial animal validation of human enzymes to determine the systemic depletion of amino acids for cancer therapy and analyze enzyme replacement for the treatment of patients having inborn metabolic defects.

The University of Texas at Austin has provided us with an option to negotiate a royalty-bearing exclusive license to any invention or discovery that is conceived or reduced to practice during the term of the Sponsored Research Agreement. Regardless of such right of first negotiation for intellectual

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property, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue a program based on that technology. We have obtained two licenses from the University of Texas at Austin. In December 2013, our wholly-owned subsidiary, AECASE, Inc. entered into an exclusive, worldwide license agreement, including the right to grant sublicenses, with the University of Texas at Austin for certain intellectual property owned by the University of Texas at Austin, including intellectual property related to the use of our product candidate AEB3103 for treatment of cancer patients. The licensed intellectual property includes an invention that was made with U.S. government support. The U.S. government therefore has certain rights in such invention under the applicable funding agreement and under applicable law. In addition, we are subject to a requirement that products covered by the agreement that are sold or used in the United States have to be manufactured substantially in the United States unless a written waiver is obtained in advance from the U.S. government. The University of Texas at Austin may terminate the license if we fail to make certain payments under the agreement. Pursuant to this license agreement, we are obligated to make payments at the achievement of certain milestones and at regular intervals throughout the life of the license. If we are in arrears in any payments due under the license, the University of Texas at Austin may terminate the agreement within 30 days after delivery of written notice to us, or if we breach any non-payment provisions of the agreement and do not cure such breach within 60 days after receiving notice of such breach, or if we have three or more financial breaches of the Agreement in any nine month period, even if we cure such breaches in the allowed period or if we or any of our affiliates or sublicensees participate in any proceeding to challenge the validity, enforceability or scope of such patent rights.

In December 2013, our wholly-owned subsidiary, AEMase, Inc. entered into an exclusive, worldwide license agreement, including the right to grant sublicenses, with the University of Texas at Austin for certain intellectual property owned by the University of Texas at Austin, including intellectual property related to the use of our product candidate AEB2109 for treatment of cancer patients. The licensed intellectual property includes an invention that was made with U.S. government support. The U.S. government therefore has certain rights in such invention under the applicable funding agreement and under applicable law. In addition, we are subject to a requirement that products covered by the agreement that are sold or used in the United States have to be manufactured substantially in the United States unless a written waiver is obtained in advance from the U.S. government. The University of Texas at Austin may terminate the license if we fail to make certain payments under the agreement. Pursuant to the license agreement, we are obligated to make payments at the achievement of certain milestones and at regular intervals throughout the life of the license. If we are in arrears in any payments due under the license, the University of Texas at Austin may terminate the agreement within 30 days after delivery of written notice to us, or if we breach any non-payment provisions of the agreement and do not cure such breach within 60 days after receiving notice of such breach, or if we have three or more financial breaches of the Agreement in any nine month period, even if we cure such breaches in the allowed period or if we or any of our affiliates or sublicensees participate in any proceeding to challenge the validity, enforceability or scope of such patent rights.

Any other licenses or other intellectual property agreements we may enter into may impose various diligence, milestone payment, royalty and other obligations on us. If we fail to comply with our obligations under current or future intellectual property agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product that is covered by the agreement or face other penalties under the agreement. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

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If we are not able to prevent disclosure of our trade secrets and other proprietary information, the value of our technology and product candidates could be significantly diminished.

We rely on trade secret protection to protect our interests in proprietary know-how and in processes for which patents are difficult to obtain or enforce. We may not be able to protect our trade secrets adequately. We have a policy of requiring our consultants, advisors and strategic partners to enter into confidentiality agreements and our employees to enter into invention, non-disclosure and non-compete agreements. However, no assurance can be given that we have entered into appropriate agreements with all parties that have had access to our trade secrets, know-how or other proprietary information. There is also no assurance that such agreements will provide for a meaningful protection of our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure of information. Furthermore, we cannot provide assurance that any of our employees, consultants, contract personnel, or strategic partners, either accidentally or through willful misconduct, will not cause serious damage to our programs and/or our strategy, for example by disclosing important trade secrets, know-how or proprietary information to our competitors. It is also possible that our trade secrets, know-how or other proprietary information could be obtained by third parties as a result of breaches of our physical or electronic security systems. Any disclosure of confidential data into the public domain or to third parties could allow our competitors to learn our trade secrets and use the information in competition against us. In addition, others may independently discover our trade secrets and proprietary information. Any action to enforce our rights is likely to be time consuming and expensive, and may ultimately be unsuccessful, or may result in a remedy that is not commercially valuable. These risks are accentuated in foreign countries where laws or law enforcement practices may not protect proprietary rights as fully as in the United States or Europe. Any unauthorized disclosure of our trade secrets or proprietary information could harm our competitive position.

Risks Related to Our Common Stock and This Offering

After this offering, our executive officers, directors and principal stockholders, if they choose to act together, will continue to have the ability to control all matters submitted to stockholders for approval.

Upon the closing of this offering, our executive officers and directors, combined with our stockholders who each owned more than 5% of our outstanding common stock before this offering will, in the aggregate, beneficially own shares representing approximately 45.3% of our capital stock based on 7,929,832 shares of common stock outstanding, on a pro forma basis, as of February 29, 2016. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of ownership control may:

- n delay, defer or prevent a change in control;
- n entrench our management and the board of directors; or
- n impede a merger, consolidation, takeover or other business combination involving us that other stockholders may desire or may result in you obtaining a premium for your shares.

Our internal control over financial reporting does not currently meet the standards required by Section 404 of the Sarbanes-Oxley Act, and failure to achieve and maintain effective internal control over financial reporting in accordance with Section 404 of the Sarbanes-Oxley Act could have a material adverse effect on our business and stock price.

We previously have not been required to maintain internal control over financial reporting in a manner that meets the standards of publicly traded companies required by Section 404(a) of the Sarbanes-Oxley Act, or Section 404(a). Internal control over financial reporting is a process designed

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to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with GAAP. We are not currently in compliance with, and we cannot be certain when we will be able to implement the requirements of Section 404(a). We may encounter problems or delays in implementing any changes necessary to make a favorable assessment of our internal control over financial reporting. If we cannot favorably assess the effectiveness of our internal control over financial reporting, or if our independent registered public accounting firm is unable to provide an unqualified attestation report on our internal controls, investors could lose confidence in our financial information and the price of our common stock could decline.

Additionally, the existence of any material weakness or significant deficiency would require management to devote significant time and incur significant expense to remediate any such material weaknesses or significant deficiencies and management may not be able to remediate any such material weaknesses or significant deficiencies in a timely manner. The existence of any material weakness in our internal control over financial reporting could also result in errors in our financial statements that could require us to restate our financial statements causing us to fail to meet our reporting obligations and cause stockholders to lose confidence in our reported financial information, all of which could materially and adversely affect us.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our certificate of incorporation and our bylaws that will become effective upon the closing of this offering may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. 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:

- n establish a classified board of directors such that only one of three classes of directors is elected each year;
- n allow the authorized number of our directors to be changed only by resolution of our board of directors;
- n limit the manner in which stockholders can remove directors from our board of directors;
- n establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- n require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- n limit who may call stockholder meetings;
- n authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- n require the approval of the holders of at least two-thirds of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our certificate of incorporation or bylaws that will become effective upon the closing of this offering.

Moreover, 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

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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 of these provisions of our charter documents or Delaware law could, under certain circumstances, depress the market price of our common stock. See Description of Capital Stock.

Our amended and restated certificate of incorporation will designate the Court of Chancery of 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, employees or agents.

Our amended and restated certificate of incorporation to be effective prior to the completion of this offering will provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or agents to us or our stockholders, any action asserting a claim arising pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws or any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein and the claim not being one which is vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery or for which the Court of Chancery does not have subject matter jurisdiction. Any person purchasing or otherwise acquiring any interest in any shares of our capital stock shall be deemed to have notice of and to have consented to this provision of our amended and restated certificate of incorporation. This choice of forum provision may limit our stockholders' ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, employees or agents, which may discourage such lawsuits against us and our directors, officers, employees and agents even though an action, if successful, might benefit our stockholders. Stockholders who do bring a claim in the Court of Chancery could face additional litigation costs in pursuing any such claim, particularly if they do not reside in or near Delaware. The Court of Chancery may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments or results may be more favorable to us than to our stockholders. Alternatively, if a court were to find this provision 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 have a material adverse effect on our business, financial condition or results of operations.

If you purchase shares of common stock in this offering, you will suffer substantial and immediate dilution of your investment.

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 after giving effect to this offering. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. To the extent shares subsequently are issued under outstanding options or other equity awards or equity securities, you will incur further dilution. Based on the initial public offering price of \$10.00 per share, you will experience immediate dilution of \$3.91 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. See Dilution.

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An active trading market for our common stock may not develop.

Prior to this offering, there has been no public market for our common stock. The initial public offering price for our common stock will be determined through negotiations with the underwriters. Although our common stock has been approved for listing on The NASDAQ Global Market, an active trading market for our shares may never develop or be sustained following this offering. If an active market for our common stock does not develop, it may be difficult for you to sell shares you purchase in this offering at a favorable price or at all.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock in this offering.

Our stock price is likely to be volatile. The stock market in general and the market for smaller biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the initial public offering price. The market price for our common stock may be influenced by many factors, including:

- n the success of competitive products or technologies;
- n results of planned clinical trials of our product candidates or those of our competitors;
- n regulatory or legal developments in the United States and other countries;
- n developments or disputes concerning patent applications, issued patents or other proprietary rights;
- n the recruitment or departure of key personnel;
- n the level of expenses related to any of our product candidates or clinical development programs;
- n the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- n actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- n operating results that fail to meet expectations of securities analysts that cover our company;
- n variations in our financial results or those of companies that are perceived to be similar to us;
- n changes in the structure of healthcare payment systems;
- n market conditions in the pharmaceutical and biotechnology sectors;
- n general economic and market conditions; and
- n the other factors described in this Risk Factors section.

We may be subject to securities litigation, which is expensive and could divert management attention.

Our stock price is likely to be volatile, and in the past companies that have experienced volatility in the market price of their stock have been subject to an increased incidence of securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

If securities or industry analysts do not publish research or reports about our business, or publish negative reports about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. There can be no assurance that analysts will cover us or provide favorable coverage. If one or more of the analysts who cover us downgrade our stock or change their opinion of our stock, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets,

which could cause our stock price or trading volume to decline.

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

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section entitled "Use of Proceeds," and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Our management could spend the net proceeds from this offering in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

A significant portion of our total outstanding shares are eligible to be sold into the 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, or the perception in the market 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 outstanding 12,929,832 shares of common stock based on the number of shares outstanding as of December 31, 2015. This includes the shares that we are selling in this offering, which may be resold in the public market immediately without restriction (including an aggregate of approximately 3,175,000 shares purchased by our existing stockholders but excluding shares purchased pursuant to the directed share program that are subject to lock-up agreements as described under "Underwriting Lock-Up Agreements"); unless purchased by our affiliates or existing stockholders. The remaining 7,929,832 shares are currently restricted as a result of securities laws or lock-up agreements but will become eligible to be sold 180 days after the offering. Moreover, after this offering, holders of an aggregate of 7,230,115 shares of our common stock will have rights, subject to specified conditions, to require us to file registration statements covering their shares to include their shares in registration statements that we may file for ourselves or other stockholders. We also intend to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described in the "Underwriting" section of this prospectus.

We are an emerging growth company, and the reduced disclosure requirements applicable to emerging growth companies may 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, and may remain an emerging growth company for up to five years. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- n 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;
- n not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting of Section 404(b) of the Sarbanes-Oxley Act;
- n not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;

n reduced disclosure obligations regarding executive compensation; and

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- n 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 not included all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we 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 will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

We are evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will first be required to furnish a report by our management on our internal control over financial reporting for the year ending December 31, 2017. As discussed above, if we cease to be an emerging growth company, we will be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm as required by Section 404(b). 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 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

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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 consolidated financial statements.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an ownership change, generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. We may have experienced an ownership change in the past, and we may experience an ownership change in connection with this offering. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership (some of which are outside of our control). As a result, if we earn net taxable income, our ability to use our pre-change NOLs and other pre-change tax attributes to offset U.S. federal taxable income or taxes may be subject to limitations, which could potentially result in increased future tax liability to us. Our NOLs and other tax attributes arising before the Conversion also may be limited by the Separate Return Limitation Year (SRLY) rule, which could increase our U.S. federal tax liability. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

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

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, appreciation, if any, in the market price of our common stock will be your sole source of gain for the foreseeable future.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including, but not limited to, the sections entitled Prospectus Summary, Risk Factors, Use of Proceeds, Management's Discussion and Analysis of Financial Condition and Results of Operations, and Business contains forward-looking statements. The words believe, may, will, potentially, estimate, continue, anticipate, target, intend, could, would, should, project, plan, expect, and similar expressions that convey uncertain events or outcomes are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

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

- n the success, cost and timing of our product candidate development activities and planned clinical trials;
- n our plans to develop and commercialize targeted therapeutics, including our lead product candidate AEB1102, for patients with an IEM and patients with cancer;
- n our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates;
- n the timing of and our ability to obtain and maintain regulatory approvals for AEB1102 and our other product candidates;
- n the rate and degree of market acceptance and clinical utility of our product candidates;
- n the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- n our commercialization, marketing and manufacturing capabilities and strategy;
- n future agreements with third parties in connection with the commercialization of our product candidates;
- n our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates;
- n regulatory developments in the United States and European and other foreign countries;
- n our ability to develop our own commercial manufacturing facility;
- n the success of competing therapies that are or may become available;
- n our ability to attract and retain key scientific or management personnel;
- n our use of the net proceeds from this offering;
- n our ability to identify additional products or product candidates with significant commercial potential that are consistent with our commercial objectives; and
- n our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in Risk Factors and elsewhere in this prospectus. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this prospectus may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected

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in the forward-looking statements will be achieved or occur. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this prospectus to conform these statements to actual results or to changes in our expectations, except as required by law.

You should read this prospectus and the documents that we reference in this prospectus and have filed with the SEC as exhibits to the registration statement of which this prospectus is a part with the understanding that our actual future results, levels of activity, performance, and events and circumstances may be materially different from what we expect.

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

We estimate that the net proceeds from our sale of shares of common stock in this offering at the initial public offering price of \$10.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately \$42.6 million, or \$49.6 million if the underwriters' option to purchase additional shares is exercised in full.

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

- n approximately \$25.0 million to fund the continuing development of AEB1102;
- n approximately \$15.0 million to fund the advancement of additional product candidates; and
- n the balance to fund working capital, including general operating expenses.

Based upon our planned use of our existing cash, cash equivalents, marketable securities and the net proceeds from this offering, we estimate such funds will be sufficient for us to fund the planned Phase 1 trial in the United States, the planned Phase 2 trial in Europe for AEB1102 for the treatment of patients with Arginase I deficiency, and to continue to fund our Phase 1 trial for AEB1102 for the treatment of solid tumors and initiate two other planned Phase 1 trials for AEB1102 for the treatment of cancer patients.

This expected use of the net proceeds from the offering represents our intentions based upon our current plans and business conditions. As of the date of this prospectus, we cannot predict with any certainty all of the particular uses for the net proceeds or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual expenditures and the extent of clinical development may vary significantly depending on numerous factors, including the status, results and timing of our current nonclinical studies and clinical trials we may commence in the future, product approval process with the FDA, EMA and MHRA, any collaborations that we may enter into with third parties and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

The expected net proceeds of this offering will not be sufficient for us to fund any of our product candidates through regulatory approval, and we will need to raise substantial additional capital to complete the development and commercialization of our product candidates.

Pending their use as described above, we plan to invest the net proceeds in short-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or guaranteed obligations of the U.S. government.

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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 for use in the operation of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant. Investors should not purchase our common stock with the expectation of receiving cash dividends.

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The following table sets forth our cash, cash equivalents and marketable securities and capitalization as of December 31, 2015:

- n on an actual basis;
- n on a pro forma basis, giving effect to (i) the automatic conversion of all outstanding shares of our convertible preferred stock into shares of common stock upon the completion of this offering and (ii) the effectiveness of our restated certificate of incorporation prior to the completion of this offering; and
- n on a pro forma as adjusted basis, giving effect to the pro forma adjustments and the sale of 5,000,000 shares of common stock by us in this offering, based on the initial public offering price of \$10.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

The pro forma as adjusted information set forth in the table below is illustrative only and will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing.

You should read this table together with the consolidated financial statements and related notes to those statements, as well as the sections of this prospectus captioned, Selected Consolidated Financial Data and Management's Discussion and Analysis of Financial Condition and Results of Operations.

	As of December 31, 2015		
	Actual	Pro Forma	Pro Forma As
	(in thousands, except share and per share data)		
			Adjusted
			(unaudited)
Cash, cash equivalents, and marketable securities	\$ 33,062	\$ 33,062	\$ 75,662
Convertible preferred stock, \$0.0001 par value; 7,180,734 shares authorized, 7,172,496 shares issued and outstanding, actual; no shares authorized, no shares issued and outstanding, pro forma and pro forma as adjusted	\$ 58,311	\$	\$
Stockholders' equity (deficit):			
Preferred stock, \$0.0001 par value: no shares authorized, no shares issued and outstanding, actual; 10,000,000 shares authorized, no shares issued and outstanding, pro forma and pro forma as adjusted			
Common stock, \$0.0001 par value: 25,000,000 shares authorized, 757,336 shares issued and outstanding, actual; 500,000,000 shares authorized, 7,929,832 shares issued and outstanding, pro forma; 500,000,000 shares authorized and 11,429,832 shares issued and outstanding, pro forma as adjusted		1	1
Additional paid-in capital	1,373	59,683	102,283

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Accumulated other comprehensive income	(1)	(1)	(1)
Accumulated deficit	(23,579)	(23,579)	(23,579)
Stockholders' (deficit) equity	(22,207)	36,104	78,704
Total capitalization	\$ 36,104	\$ 36,104	\$ 78,704

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The number of shares of our common stock issued and outstanding as set forth in the table above excludes:

- n 629,848 shares of common stock issuable upon the exercise of options granted as of December 31, 2015, with a weighted-average exercise price of \$4.55 per share;
- n 84,417 shares of common stock issuable upon the exercise of options granted since January 1, 2016, with a weighted-average exercise price of \$5.46 per share; and
- n 1,859,286 shares of common stock reserved for future issuance under our stock-based compensation plans as of December 31, 2015, consisting of (a) 594,286 shares of common stock reserved for future issuance under our 2015 Equity Incentive Plan, (b) 1,100,000 shares of common stock reserved for future issuance under our 2016 Equity Incentive Plan, which became effective on the date immediately prior to the date of this prospectus and (c) 165,000 shares of common stock reserved for future issuance under our 2016 Employee Stock Purchase Plan, which became effective on the date of this prospectus. Upon completion of this offering, any remaining shares available for issuance under our 2015 Equity Incentive Plan will be added to the shares reserved under our 2016 Equity Incentive Plan and we will cease granting awards under our 2015 Equity Incentive Plan. Our 2016 Equity Incentive Plan also provides for automatic annual increases in the number of shares reserved under the plan each year, as more fully described in Executive Compensation Employee Benefit and Stock Plans.

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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 and the pro forma as adjusted net tangible book value per share of common stock immediately after this offering.

As of December 31, 2015, our historical net tangible book value was approximately \$36.1 million, or \$47.67 per share of common stock. Our historical net tangible book value per share represents the amount of our total tangible assets reduced by the amount of our total liabilities divided by the total number of shares of our common stock outstanding as of December 31, 2015.

As of December 31, 2015, our pro forma net tangible book value was approximately \$36.1 million, or \$4.55 per share of common stock. Our pro forma net tangible book value per share represents the amount of our total tangible assets reduced by the amount of our total liabilities and divided by the total number of shares of our common stock outstanding as of December 31, 2015, giving effect to the automatic conversion of all outstanding shares of our convertible preferred stock into 7,172,496 shares of common stock upon the completion of this offering.

After giving effect to our sale in this offering of 5,000,000 shares of our common stock, at the initial public offering price of \$10.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of December 31, 2015 would have been approximately \$78.7 million, or \$6.09 per share of our common stock. This represents an immediate increase in pro forma as adjusted net tangible book value of \$1.53 per share to our existing stockholders and an immediate dilution of \$3.91 per share to investors purchasing shares in this offering, as follows:

Initial public offering price per share	\$ 10.00
Pro forma net tangible book value per share as of December 31, 2015	\$ 4.55
Pro forma increase in net tangible book value per share as of December 31, 2015 attributable to new investors	\$ 1.53

Pro forma as adjusted net tangible book value per share after this offering	6.09
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Dilution in pro forma as adjusted net tangible book value per share to investors in this offering	\$ 3.91
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If the underwriters exercise their option to purchase 750,000 additional shares in full, the pro forma as adjusted net tangible book value per share of our common stock after giving effect to this offering would be \$6.26 per share, representing an immediate increase in the pro forma as adjusted net tangible book value to existing stockholders of \$1.71 per share and an immediate dilution of \$3.74 per share to new investors participating in this offering.

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The following table summarizes, on a pro forma as adjusted basis as of December 31, 2015 after giving effect to (i) the automatic conversion of all outstanding shares of our convertible preferred stock into 7,172,496 shares of common stock upon the completion of this offering; and (ii) this offering at the initial public offering price of \$10.00 per share, the difference between existing stockholders and new investors with respect to the number of shares of common stock purchased from us, the total consideration paid to us, and the average price per share paid, before deducting underwriting discounts and commissions and estimated offering expenses payable by us (in thousands, except per share amounts and percentages):

	Shares Purchased		Total Consideration		Average Price
	Number	Percent	Amount	Percent	per Share
Existing stockholders	7,929,832	61.3%	\$ 59,683,795	54.4%	\$ 7.53
New public investors	5,000,000	38.7%	50,000,000	45.6%	\$ 10.00
Total	12,929,832	100%	\$ 109,683,795	100%	

Except as otherwise indicated, the above discussion and tables assume no exercise of the underwriters' option to purchase additional shares. If the underwriters exercise their option to purchase additional in full, our existing stockholders would own 58.0% and our new investors would own 42.0% of the total number of shares of our common stock outstanding upon the completion of this offering.

To the extent that any outstanding options are exercised, investors will experience further dilution.

Certain of our existing stockholders or their affiliates have agreed to purchase an aggregate of approximately 3,175,000 shares of our common stock in this offering at the initial public offering price. In addition, the information in this section does not reflect the potential purchases of shares reserved for the directed share program.

The number of shares of our common stock to be outstanding after this offering is based on 7,929,832 shares of our common stock outstanding, on a pro forma basis, as of December 31, 2015 and excludes:

- n 629,848 shares of common stock issuable upon the exercise of options granted as of December 31, 2015, with a weighted-average exercise price of \$4.55 per share;
- n 84,417 shares of common stock issuable upon the exercise of options granted since January 1, 2016, with a weighted-average exercise price of \$5.46 per share; and
- n 1,859,286 shares of common stock reserved for future issuance under our stock-based compensation plans as of December 31, 2015, consisting of (a) 594,286 shares of common stock reserved for future issuance under our 2015 Equity Incentive Plan, (b) 1,100,000 shares of common stock reserved for future issuance under our 2016 Equity Incentive Plan, which became effective on the date immediately prior to the date of this prospectus and (c) 165,000 shares of common stock reserved for future issuance under our 2016 Employee Stock Purchase Plan, which became effective on the date of this prospectus. Upon completion of this offering, any remaining shares available for issuance under our 2015 Equity Incentive Plan will be added to the shares reserved under our 2016 Equity Incentive Plan and we will cease granting awards under our 2015 Equity Incentive Plan. Our 2016 Equity Incentive Plan also provides for automatic annual increases in the number of shares reserved under the plan each year, as more fully described in Executive Compensation Employee Benefit and Stock Plans.

Table of Contents**SELECTED CONSOLIDATED FINANCIAL DATA**

The following selected consolidated financial data should be read together with our consolidated financial statements and related notes and Management's Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this prospectus. The selected consolidated financial data in this section are not intended to replace our consolidated financial statements and the related notes. We derived the consolidated statement of operations data for years ended December 31, 2014 and 2015, and the consolidated balance sheet data as of December 31, 2014 and 2015 from our audited consolidated financial statements and related notes appearing elsewhere in this prospectus. The consolidated statement of operations data for the period from December 16, 2013 (inception) through December 31, 2013 are derived from audited financial statements not included in this prospectus. Our historical results are not necessarily indicative of the results that may be expected in the future.

	Period from December 16, 2013 (Inception) through December 31, 2013	Year Ended December 31,				
		2014	2015			
	(in thousands, except share and per share amounts)					
Consolidated Statements of Operations Data:						
Revenues:						
Grant	\$	\$	\$	6,085		
Operating expenses:						
Research and development	\$	1,150	\$	6,830	\$	11,453
General and administrative		735		2,074		5,947
Total operating expenses		1,885		8,904		17,400
Loss from operations		(1,885)		(8,904)		(11,315)
Other income (expense):						
Interest income				1		22
Change in fair value of forward sale contract		(52)		(1,444)		
Other expense, net						(2)
Total other income (expense):		(52)		(1,443)		20
Net loss	\$	(1,937)	\$	(10,347)	\$	(11,295)
Deemed dividend to convertible preferred stockholders						(228)
Net loss allocable to common shareholders and stockholders	\$	(1,937)	\$	(10,347)	\$	(11,523)
Common A-1 shares:						
Basic and diluted net loss per share	\$	(15.48)	\$	(20.13)	\$	
Net loss attributable to class	\$	(1,277)	\$	(3,321)	\$	
Basic and diluted weighted-average shares outstanding		82,500		165,000		

Common A shares:

Basic and diluted net loss per share	\$	(3.94)	\$	(17.06)	\$
Net loss attributable to class	\$	(660)	\$	(5,706)	\$
Basic and diluted weighted-average shares outstanding		167,261		334,522	

Common B shares:

Basic and diluted net loss per share	\$		\$	(40.17)	\$
Net loss attributable to class	\$		\$	(1,320)	\$
Basic and diluted weighted-average shares outstanding				32,861	

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	Period from December 16, 2013 (Inception) through December 31, 2013	Year Ended December 31, 2014			2015
	(in thousands, except share and per share amounts)				
Common Stock:					
Basic and diluted net loss per share allocable to common stockholders	\$	\$	\$		(19.21)
Net loss allocable to common stockholders	\$	\$	\$		(11,523)
Basic and diluted weighted-average shares outstanding					599,788
Pro forma net loss per share (unaudited)(1)					
Basic and diluted net loss per share			\$		(1.69)
Basic and diluted weighted-average shares outstanding					6,820,042

(1) Refer to Note 12 of our consolidated financial statements for the year ended December 31, 2015 appearing elsewhere in this prospectus, for a description of the method used to calculate our unaudited pro forma basic and diluted net loss per share, unaudited supplemental pro forma basic and diluted net loss per share and weighted-average shares outstanding used to calculate the per share amounts.

	As of December 31, 20142015 (in thousands)	
Consolidated Balance Sheet Data:		
Cash, cash equivalents, and marketable securities	\$ 2,616	\$ 33,062
Working capital	1,672	35,763
Total assets	2,930	38,654
Total liabilities	1,058	2,550
Convertible preferred shares	13,345	58,311
Accumulated deficit	(12,284)	(23,579)
Total members and stockholders deficit	(11,473)	(22,207)

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MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis should be read in conjunction with Selected Consolidated Financial Data and our consolidated financial statements and related notes included elsewhere in this prospectus. In the case of the period from December 16, 2013 (inception) to December 31, 2013 and as of December 31, 2013, our consolidated financial statements are not included in this prospectus. This discussion and analysis and other parts of this prospectus contain forward-looking statements based upon current beliefs, plans and expectations that involve risks, uncertainties and assumptions, such as statements regarding our plans, objectives, expectations, intentions and projections. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under Risk Factors and elsewhere in this prospectus. You should carefully read the Risk Factors section of this prospectus to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Please also see the section entitled Special Note Regarding Forward-Looking Statements.

Overview

We are a biotechnology company committed to developing enzyme-based therapeutics in the field of amino acid metabolism that we believe will transform the lives of patients with inborn errors of metabolism and cancer. Our engineered human enzymes are designed to reduce the level of specific amino acids in the blood. In inborn errors of metabolism, or IEM, a subset of rare genetic metabolic diseases, we are seeking to reduce the toxic levels of amino acids in patients. In oncology, we are seeking to reduce amino acid blood levels below the normal range where we believe we will be able to exploit the dependence of certain cancers on specific amino acids.

Our lead product candidate, AEB1102, is engineered to degrade the amino acid arginine and is being developed to treat two extremes of arginine metabolism, including arginine excess in patients with Arginase I deficiency, an IEM, as well as some cancers which have shown to have a metabolic dependence on arginine. AEB1102 has demonstrated the ability to reduce blood arginine levels in nonclinical and clinical studies supporting its use as a potential treatment of both Arginase I deficiency and cancer.

We were formed as a limited liability company under the laws of the State of Delaware in December 2013 and converted to a Delaware corporation in March 2015. In connection with our conversion to a Delaware corporation, each of our outstanding shares of the members of the limited liability company was converted into shares of capital stock. On the date of conversion, the following conversions of limited liability shares took place: (i) each Series A convertible preferred share converted into one share of Series A convertible preferred stock, par value \$0.0001 per share; (ii) each Common A share converted into one share of common stock, par value \$0.0001 per share; (iii) each Common A-1 share converted into one share of common stock, par value \$0.0001 per share; (iv) each Common B share with a threshold amount of \$12.2 million converted into 0.7576 shares of common stock and a grant of 0.2424 options to acquire one share of common stock; and (v) each Common B share with a threshold amount of \$22.1 million converted into 0.4242 shares of common stock and a grant of 0.5758 options to acquire one share of common stock. The threshold amount represents the amount which any distribution must cumulatively exceed before holders of the Common B shares participate pro rata with the holders of the Series A convertible preferred shares and Common A-1 and A shares in such distribution; however, holders of the Series A convertible preferred shares and Common A-1 and A shares are entitled to receive their distribution priority before the holders of the Common B shares would receive proceeds from any distribution.

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Since inception, we have devoted substantially all of our efforts and resources to identifying and developing product candidates, conducting nonclinical studies and initiating clinical trials, recruiting personnel and raising capital. To date, we have financed our operations primarily through the sale and issuance of convertible preferred and common equity securities and the collection of a research grant. We have no recorded revenue from product sales and all of our revenue to date has been grant revenue. Since our inception, and through December 31, 2015, we have raised an aggregate of \$54.7 million to fund our operations through sale and issuance of convertible preferred and common equity securities and collection of \$4.4 million in grant proceeds.

We have incurred net losses in each year since inception. Our net losses were \$1.9 million, \$10.3 million and \$11.3 million for the period from December 16, 2013 (inception) through December 31, 2013 and the years ended December 31, 2014 and 2015, respectively. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative expenses associated with our operations. Our cash, cash equivalents, and marketable securities balance as of December 31, 2015 totaled \$33.1 million.

Components of Operating Results

Revenue

To date, we have recognized revenue solely from a research grant and have not generated any product revenue. Our ability to generate product revenues, which we do not expect will occur for several years, if ever, will depend heavily on the successful development, regulatory approval and eventual commercialization of our product candidates.

In June 2015, we entered into a grant agreement with the Cancer Prevention and Research Institute of Texas, or CPRIT, for \$19.8 million covering a three year period from June 1, 2014 through May 31, 2017. The grant allows us to receive funds in advance of costs and allowable expenses being incurred. We record the revenue as qualifying costs are incurred and there is reasonable assurance that the conditions of the award have been met for collection. Proceeds received prior to the costs being incurred are recognized as deferred revenue until the services are performed.

On a quarterly basis, we are required to submit a financial reporting package outlining the nature and extent of reimbursable costs paid and requesting reimbursement under the grant. At the end of each period, expenses paid prior to reimbursement result in the recognition of a grant receivable.

Research and development expenses

Research and development expenses consist primarily of costs incurred for the discovery and development of our product candidates, most notably, our lead product candidate AEB1102. Since we currently do not have internal laboratory or manufacturing capabilities, we contract with external providers for nonclinical studies, clinical trials and manufacturing services. Our research and development costs include:

- n costs from acquiring clinical trial materials and services performed for contracted services with our strategic manufacturing partner;
- n fees paid to clinical trial sites, clinical research organizations, contract research organizations, contract manufacturing organizations, nonclinical research supply companies, and academic institutions;
- n acquired in process research and development at inception;
- n

employee and consultant-related expenses incurred, which include salaries, benefits, travel and share-based compensation; and

n expenses incurred under license agreements with third parties.

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Research and development costs are expensed as incurred. Advance payments for goods or services to be rendered in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

Research and development costs have historically represented the largest component of our total operating expenses. We plan to increase our research and development expenses for the foreseeable future as we continue the development of our product candidates.

Our expenditures on current and future nonclinical and clinical development programs are subject to numerous uncertainties in timing and cost to completion. The duration, costs, and timing of clinical trials and development of our product candidates will depend on a variety of factors, including:

- n the scope, rate of progress, and expenses of our ongoing research activities as well as any additional clinical trials and other research and development activities;
- n future clinical trial results;
- n uncertainties in clinical trial enrollment rates or drop-out or discontinuation rates of patients;
- n potential safety monitoring or other studies requested by regulatory agencies;
- n significant and changing government regulation; and
- n the timing and receipt of regulatory approvals, if any.

The process of conducting the necessary clinical research to obtain FDA and other regulatory approval is costly and time consuming and the successful development of our product candidates is highly uncertain. The risks and uncertainties associated with our research and development projects are discussed more fully in the section of this prospectus titled Risk Factors. As a result of these risks and uncertainties, we are unable to determine with any degree of certainty the duration and completion costs of our research and development projects, 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.

At inception, we acquired in-process research and development assets, consisting of patents and know-how used in connection with the development, manufacture, and commercialization of technology and future products incorporating the assigned intellectual property rights, from one of our founders in an asset acquisition. The in-process research and development assets were expensed immediately as research and development costs. As consideration for the assets, we issued 165,000 Common A-1 shares with a fair value of \$277,000 and 200,714 Common A shares with a fair value of \$232,000, and reimbursed prior intellectual property expenses of \$237,000. As of December 31, 2013, 2014 and 2015, we had an outstanding liability to or on behalf of the founder of \$253,000, \$0 and \$0, respectively.

General and administrative expenses

General and administrative expenses consist primarily of salaries and other related costs, including share-based compensation, for personnel in executive, finance, accounting, and human resources functions. Other significant costs include legal fees relating to intellectual property and corporate matters and fees for accounting and consulting services.

We anticipate that our general and administrative expenses will increase in the future to support our continued research and development activities, potential commercialization of our product candidates and the increased costs of operating as a public company. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, among other expenses. Additionally, we anticipate

increased costs

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associated with being a public company, including expenses related to services associated with maintaining compliance with NASDAQ listing rules and SEC requirements, insurance and investor relations costs.

Interest income

Interest income consists of interest earned on our cash, cash equivalents, and marketable securities.

Loss on forward contract

The financing arrangement in connection with the sale and issuance of our Series A convertible preferred shares included a second closing in July 2014, which, for financial reporting purposes, resulted in a contract for the forward sale of an additional 837,594 Series A convertible preferred shares at a price of \$5.25 per share, contingent upon certain milestones being met. This freestanding financial instrument was classified as a liability because the underlying preferred shares are contingently redeemable. The forward sale contract was carried at fair value on the balance sheet, with changes in fair value recorded in earnings. The changes in fair value of the derivative liability from our inception through settlement in July 2014 were recorded as other income (expense) in the consolidated statements of operations.

Income taxes

Since inception in December 2013, through March 10, 2015, we were a Delaware LLC and elected to file as a partnership for federal and state income tax purposes for the period from December 16 (inception) through December 31, 2013 and for the year ended December 31, 2014. Our taxable losses from inception through December 31, 2014 were allocated to the members in accordance with the LLC operating agreement. Accordingly, income taxes have not been provided for the period from December 16 (inception) through December 31, 2013 and the year ended December 31, 2014, as the losses are included in the members' federal income tax returns. On March 10, 2015, we converted from a Delaware LLC to a Delaware corporation, and will file a corporate income tax return for the year ended December 31, 2015. For tax purposes, we elected to be treated as a corporation under Subchapter C of Chapter 1 of the United States Internal Revenue Code, effective January 1, 2015. We therefore, are subject to federal and state tax expense beginning January 1, 2015.

We serve as a holding company for our seven wholly-owned subsidiary corporations that filed individual income tax returns at the federal and state level for the period from December 16 (inception) through December 31, 2013 and the year ended December 31, 2014. For the year ended December 31, 2015, we and our seven wholly-owned subsidiaries will file a consolidated corporate federal income tax return. We use the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the financial statements and the tax bases of assets and liabilities. A valuation allowance is established against the deferred tax assets to reduce their carrying value to an amount that is more likely than not to be realized. Due to our lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance.

We recognize benefits of uncertain tax positions if it is more likely than not that such positions will be sustained upon examination based solely on the technical merits, as the largest amount of benefits that is more likely than not to be realized upon the ultimate settlement. Our policy is to recognize interest and penalties related to the unrecognized tax benefits as a component of income tax expense. To date, there have been no interest or penalties charged in relation to the unrecognized tax benefits.

Table of Contents**Results of Operations****Comparison of the years ended December 31, 2014 and 2015**

The following table summarizes our results of operations for the years ended December 31, 2014 and 2015, together with the changes in those items in dollars and as a percentage:

	Year Ended December 31,		Dollar	% Change
	2014	2015	Change	
	(dollars in thousands)			
Revenues:				
Grant	\$	\$ 6,085	\$ 6,085	*
Operating expenses:				
Research and development	\$ 6,830	\$ 11,453	\$ 4,623	68%
General and administrative	2,074	5,947	3,873	187%
Total operating expenses	8,904	17,400	8,496	95%
Loss from operations	(8,904)	(11,315)	(2,411)	27%
Interest income	1	22	21	*
Change in fair value of forward sale contract	(1,444)		1,444	*
Other expense, net		(2)	(2)	*
Net loss	\$ (10,347)	\$ (11,295)	\$ (948)	9%

* Percentage not meaningful

Grant Revenues. We recorded grant revenue of \$6.1 million for the year ended December 31, 2015, including \$2.0 million in revenue for qualifying 2014 expenditures. Upon execution of the CPRIT grant agreement in June 2015, grant revenue was recognized for the accumulated qualified expenditures paid and recognized in the period from June 1, 2014 through June 30, 2015.

Research and Development Expenses. Research and development expenses increased by \$4.6 million to \$11.4 million in 2015 from \$6.8 million in 2014, an increase of 68%. Included in the research and development expenses are costs directly associated with our lead product candidate AEB1102, which increased to \$7.0 million in 2015 from \$3.7 million in 2014. The increase in research and development expenses was primarily due to:

- n Higher nonclinical expenses, which increased by \$1.8 million as a result of increased diagnostic-related costs in preparation for clinical trials related to AEB1102 and additional research with the University of Texas at Austin;
- n Higher personnel-related expenses, which increased by \$1.3 million as a result of increased headcount in preparation for the initiation of clinical trials for AEB1102;
- n

Higher clinical development expenses, which increased by \$0.8 million primarily as a result of initiating our Phase 1 dose escalation trial in patients with advanced solid tumors for AEB1102;

- n Higher consulting expenses, which increased by \$0.4 million as a result of our greater nonclinical and clinical development efforts in 2015; and
- n Higher clinical regulatory-related expenses, which increased by \$0.3 million as a result of greater expenses incurred in 2015 for the preparation and submission of two investigational new drug applications with the FDA for AEB1102 for the treatment of solid tumors and Arginase I deficiency.

General and Administrative Expenses. General and administrative expenses increased by \$3.9 million to \$6.0 million in 2015 from \$2.1 million in 2014, an increase of 187%. The increase in general and administrative expenses was primarily due to an increase of \$1.9 million in employee compensation, recruiting, and travel expenses and \$1.6 million in professional services, audit and legal

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fees associated with preparing to be a public company and the development of administrative functions. In addition, facility-related costs increased by \$0.3 million due to moving to a larger office in January 2015.

Interest Income. Interest income consists of interest earned on our cash, cash equivalents, and marketable securities. The increase in interest income in 2015 to \$22,000 from \$1,000 in 2014 was primarily due to funds invested from closing the Series B convertible preferred stock financing in March 2015.

Loss on Forward Contract. The loss on forward contract consisted of changes in the fair value of the forward contract that was issued upon the first closing of the Series A convertible preferred shares in December 2013. The forward sale contract was settled on July 15, 2014 when the company issued and received payment for additional Series A convertible preferred shares.

Comparison of the Period from December 16, 2013 (inception) to December 31, 2013 and the year ended December 31, 2014

Research and development expenses

Research and development expenses for the period from December 16, 2013 (inception) to December 31, 2013 were \$1.1 million and primarily consisted of \$0.5 million of a non-cash charge to record the acquisition of in-process research and development, \$0.3 million for related legal and license fees, \$0.2 million for initial manufacturing of our lead product candidate and \$0.1 million for preclinical expenditures.

Research and development expenses for the year ended December 31, 2014 were \$6.8 million and primarily consisted of \$2.7 million in manufacturing costs, including \$0.8 million in non-cash charges from Series A convertible preferred shares issued for services performed, \$2.2 million in nonclinical expenses including those related to our sponsored research, \$1.3 million in compensation for employees and consultants and \$0.5 million for a non-cash discount on the issuance of Series A convertible preferred shares to other investors and employees of the company. In 2014, \$3.7 million of research and development expenses were directly associated with the development of our lead product candidate, AEB1102.

General and administrative expenses

General and administrative expenses for the period from December 16, 2013 (inception) to December 31, 2013 were \$0.7 million and consisted primarily of \$0.4 million of employee and consultant compensation and travel and \$0.3 million of legal expenses.

General and administrative expenses for the year ended December 31, 2014, were \$2.1 million and consisted primarily of \$1.6 million in compensation and travel expenses for employees and consultants and \$0.2 million in professional and legal fees.

Loss on forward contracts

Loss on forward contracts was \$52,000 and \$1.4 million for the period from December 16, 2013 (inception) to December 31, 2013 and the year ended December 31, 2014, respectively, and consisted of changes in the fair value of the forward contract that resulted from the second closing of the Series A financing. See Note 6 of Notes to Consolidated Financial Statements.

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Liquidity and Capital Resources

Sources of liquidity

We are an early stage biotechnology company with a limited operating history, and due to our significant research and development expenditures, we have generated operating losses since our inception. Through December 31, 2015, we have funded our operations by raising an aggregate of \$54.7 million of gross proceeds from the sale and issuance of convertible preferred and common equity securities and collected \$4.4 million in grant proceeds. We have not generated any revenue from the sale of any products. Additionally, we entered into an agreement with our strategic manufacturing partner to provide convertible preferred shares in exchange for services performed.

In June 2015, we entered into a Cancer Research Grant Contract with CPRIT, under which we expect to generate up to \$19.8 million in grant funding to fund our development of AEB1102. As of December 31, 2015, we have a grant receivable outstanding of \$1.7 million. For a detailed discussion of this grant, see Business Grant Agreement.

Our primary use of cash is to fund the development of our lead product candidate, AEB1102. This includes both the research and development costs and the general and administrative expenses required to support those operations. Since we are an early stage company, we have incurred significant operating losses since our inception and we anticipate such losses, in absolute dollar terms, to increase as we continue our clinical trials in AEB1102 and expand our development efforts in our pipeline of nonclinical candidates.

As of December 31, 2015, we had available cash, cash equivalents, and marketable securities of \$33.1 million. We believe that we have sufficient resources to fund our operations through June 30, 2017.

Future funding requirements and operational plan

Our operational plan for the current and upcoming fiscal years ending December 31, 2016 and December 31, 2017, respectively, is to continue and commence clinical trials for our lead product candidate AEB1102 in two separate indications, oncology and Arginase I deficiency, and to expand development for at least one additional product candidate. As such, we plan to increase our research and development expenditures for the foreseeable future with nonclinical studies, clinical trials, manufacturing and an integrated biomarker strategy. We expect our principal expenditures during this time period to include expenses for the following:

- n funding the continuing development of AEB1102;
- n funding the advancement of any of additional product candidates; and
- n funding working capital, including general operating expenses.

We anticipate that we will continue to generate losses into the foreseeable future as we develop our lead product candidates, seek regulatory approval of those candidates and begin to commercialize any approved products. Until such time as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity or debt financings and research grants. We currently have no debt or debt facility or additional committed capital. To the extent that we raise additional equity, the ownership interest of our shareholders will be diluted.

Due to our significant research and development expenditures, we have generated substantial losses in each period since inception. We have incurred an accumulated deficit of \$23.6 million through December 31, 2015. We expect to incur substantial losses in the future as we expand our research and development capabilities. Based on those plans, we expect that the net proceeds from this

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offering, together with our existing cash, will enable us to fund our operating expenses and capital expenditure requirements for at least the next 24 months. We have based this estimate on assumptions that may prove to be incorrect, however, and we could use our capital resources sooner than we expect.

Cash flows

The following table summarizes our cash flows for the periods indicated (in thousands):

	Period from December 16, 2013 (Inception) through December 31, 2013	Year Ended December 31, 2014	2015
Net cash used in operating activities	\$ (301)	\$ (7,335)	\$ (10,982)
Net cash used in investing activities		(221)	(4,014)
Net cash provided by financing activities	4,898	5,575	41,674
Net (decrease) increase in cash	\$ 4,597	\$ (1,981)	\$ 26,678

Cash used in operating activities

Cash used in operating activities for the period December 16, 2013 (inception) through December 31, 2013 was \$0.3 million and reflected a net loss of \$1.9 million, offset in part by non-cash charges of \$0.5 million related to acquisition of in-process research and development from our scientific founder, and an increase of \$0.9 million of accounts payable and accrued expenses.

Cash used in operating activities for the year ended December 31, 2014 was \$7.3 million and reflected a net loss of \$10.3 million, offset in part by non-cash expenses of \$1.4 million for the change in fair value of the forward contracts associated with the second closing of the Series A financing, \$0.8 million for convertible preferred shares issued to our strategic manufacturing partner in exchange for services performed, \$0.5 million for the discount on the sale of convertible preferred shares and \$0.1 million of share based compensation.

Cash used in operating activities for the year ended December 31, 2015 was \$11.0 million and reflected a net loss of \$11.3 million, offset in part by non-cash expenses of \$0.8 million for stock-based compensation and \$0.8 million for convertible preferred shares issued to our strategic manufacturing partner in exchange for services performed. Cash used in operating activities also reflected an increase of \$1.7 million in grant accounts receivable from executing the grant agreement in 2015 and \$0.6 million in prepaid expenses and other assets driven by an increase in prepaid research and development costs, offset by a \$1.1 million increase in accrued and other liabilities driven by an increase in accrued research and development costs, consulting and legal accruals.

Cash used in investing activities

Cash used in investing activities for the year ended December 31, 2014 was \$0.2 million and consisted primarily of capital purchases of computer and laboratory equipment.

Cash used in investing activities for the year ended December 31, 2015 was \$4.0 million and consisted of \$208,000 in purchases of property and equipment, an increase in restricted cash of \$40,000 and \$3.8 million in purchases of marketable securities.

Cash provided by financing activities

Cash provided by financing activities for the period December 16, 2013 (inception) through December 31, 2013 was \$4.9 million resulting from proceeds on the first closing of the Series A

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financing in December 2013 of \$4.5 million and \$0.4 million in proceeds allocated to the issuance of the forward sale contract on Series A convertible preferred shares associated with the second closing of the Series A financing.

Cash provided by financing activities for the year ended December 31, 2014 was \$5.6 million, resulting from the second closing of the Series A financing in July 2014.

Cash provided by financing activities for the year ended December 31, 2015 was \$41.7 million resulting from \$44.0 million from the closing of the Series B financing in March 2015, offset by \$0.3 million in Series B issuance costs and \$2.0 million in offering costs related to our proposed initial public offering of our common stock.

Contractual Obligations

The following table summarizes our contractual obligations as of December 31, 2015 (in thousands):

		Payments Due by Period			
		Less than 1 year	1 to 3 years	4 to 5 years	More than 5 years
Operating leases	\$ 140	\$ 144	\$	\$	
Sponsored research agreement	375				
Total contractual obligations	\$ 515	\$ 144	\$	\$	

The above contractual obligations result from a non-cancellable lease agreement for our office space in Austin, Texas. In August 2015, we amended our research agreement with the University of Texas at Austin to extend the period of performance and increase the limitation of funding to perform additional research. Under the terms of the amendment, the performance period was extended to August 15, 2016 for \$0.6 million with \$0.4 million expected to be paid in 2016.

Contingent contractual obligations

We do not have any milestone or royalty obligations with respect to our lead product candidate, AEB1102.

On December 24, 2013, two of our wholly owned subsidiaries, AECASE, Inc. (AECASE) and AEMASE, Inc. (AEMASE) entered into license agreements with the University of Texas at Austin (UTA) under which UTA has granted to AECASE and AEMASE exclusive, worldwide, sublicenseable licenses. UTA granted the AECASE license under a patent application relating to the right to use technology related to our AEB3103 product candidate. UTA granted the AEMASE license under a patent relating to the right to use technology related to our AEB2109 product candidate.

The licenses have substantially identical terms. With respect to each product candidate covered by a license with UTA, AECASE or AEMASE could be required to pay UTA up to \$6.4 million milestone payments based on the achievement of certain development milestones, including clinical trials and regulatory approvals, the majority of which are due upon the achievement of later development milestones, including a \$5.0 million payment due on regulatory approval of a product and a \$500,000 payment payable on final regulatory approval of a product for a second indication. AECASE and AEMASE are also required to pay an annual license fee, ranging from \$5,000 to \$25,000. In addition, AECASE and AEMASE will pay UTA a low single digit royalty on worldwide-net sales of

products covered under each license agreement, together with a revenue share on non-royalty consideration received from sublicensees. The rate of the revenue share depends on the date the sublicense agreement is signed. The rate is 30% for agreements signed in 2014, 25% for agreements signed in 2015, 20% for agreements signed in 2016, 15% for agreements signed in 2017 and 6.5% for

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agreements signed in 2018 and thereafter. UTA may terminate the agreement for breach by AECASE or AEMASE that is not cured within 30 or 60 days of notice (depending on the type of breach) and three or more financial breaches in any nine month period which, even if cured, were not cured within 30 days of notice, or if AECASE or AEMASE or any of their respective affiliates or sublicensees participates in any proceeding to challenge the licensed patent rights (unless, with respect to sublicensees, AECASE or AEMASE terminates the applicable sublicense).

Off Balance Sheet Arrangements

We do not have any off balance sheet arrangements, as defined by applicable SEC regulations.

Recent Accounting Pronouncements

In August 2014, the FASB issued ASU 2014-15, *Presentation of Financial Statements – Going Concern (Subtopic 205-40): Disclosure of uncertainties about an Entity’s Ability to continue as a Going Concern*, which provides guidance on the presentation of management’s plans, when conditions or events raise substantial doubt about the entity’s ability to continue as a going concern within one year after the date that the financial statements are issued. The new standard is effective for fiscal years ending after December 15, 2016. The adoption of this standard is not expected to have a material impact on our financial statements.

In April 2015, the FASB issued ASU No. 2015-05, *Intangibles-Goodwill and Other-Internal-Use Software (Subtopic 350-40): Customer’s Accounting for Fees Paid in a Cloud Computing Arrangement*, which provides guidance over a customer’s accounting for fees paid in a cloud computing arrangement. The guidance is effective for annual periods beginning after December 15, 2015. The adoption will have no impact on the Company’s financial statements.

In November 2015, the FASB issued ASU No. 2015-17, *Income Taxes (Topic 740): Balance Sheet Classification of Deferred Taxes*, which requires classification of all deferred tax assets and liabilities as noncurrent on the balance sheet instead of separating deferred taxes into current and noncurrent amounts. In addition, companies will no longer allocate valuation allowances between current and noncurrent deferred tax assets because those allowances will also be classified as noncurrent. This guidance is effective for annual periods beginning after December 15, 2017. Early adoption is permitted. The amendments can be applied either prospectively or retrospectively. The standard will be adopted beginning with the year ended December 31, 2015. Adoption of this guidance did not affect our historical consolidated financial statements.

Emerging Growth Company Status

We are an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act, and therefore we may take advantage of certain exemptions from various public company reporting requirements. As an emerging growth company:

- n we will present no more than two years of audited financial statements and no more than two years of related management’s discussion and analysis of financial condition and results of operations;
- n we will avail ourselves of the exemption from the requirement to obtain an attestation and report from our auditors on the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act;
- n we will provide less extensive disclosure about our executive compensation arrangements; and
- n we will not require stockholder non-binding advisory votes on executive compensation or golden parachute arrangements.

In addition, the JOBS Act permits an emerging growth company such as ours to delay the adoption of new or revised accounting standards applicable to public companies until such standards are made

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applicable to private companies. We have chosen irrevocably to not avail ourselves of this extended transition period for complying with new or revised accounting standards, 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 will remain an emerging growth company for up to five years, although we will cease to be an emerging growth company upon the earliest of: (1) the last day of the fiscal year following the fifth anniversary of this offering, (2) the last day of the first fiscal year in which our annual gross revenues are \$1 billion or more, (3) the date on which we have, during the previous rolling three-year period, issued more than \$1 billion in non-convertible debt securities and (4) the date on which we are deemed to be a large accelerated filer as defined in the Exchange Act.

Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2015, we held \$33.1 million in cash, cash equivalents, and marketable securities, all of which was denominated in U.S. dollar assets, and consisting primarily of investments in reverse repurchase agreements and U.S government and agency 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 marketable securities. Our marketable securities are subject to interest rate risk and could 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 10% change in interest rates would not have a material effect on the fair market value of our investment portfolio. We have the ability to hold our marketable securities until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of these financial statements requires us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities as of the dates of the balance sheets and the reported amounts of expenses during the reporting periods. In accordance with GAAP, we base our estimates on historical experience and on various other assumptions that we believe are reasonable under the circumstances at the time such estimates are made. Actual results may differ materially from our estimates and judgments under different assumptions or conditions. We periodically review our estimates in light of changes in circumstances, facts and experience. The effects of material revisions in estimates are reflected in our consolidated financial statements prospectively from the date of the change in estimate.

We define our critical accounting policies as those accounting principles generally accepted in the United States that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations, as well as the specific manner in which we apply those principles. Our significant accounting policies are more fully described in Note 2 to our audited consolidated financial statements appearing elsewhere in this prospectus.

Accrued research and development costs

We record the costs associated with research nonclinical studies, clinical trials and manufacturing development as incurred. These costs are a significant component of our research and development

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expenses, as a substantial portion of our on-going research and development activities are conducted by third-party service providers, including contract research organizations and manufacturing activities.

We accrue for expenses resulting from obligations under contracts with contract research organizations, or CROs, contract manufacturing organizations, or CMOs, and other outside service providers for which payment flows do not match the periods over which materials or services are provided to us. We record accruals based on estimates of services received and efforts expended pursuant to agreement established with CROs, CMOs and other outside service providers. These estimates are typically based on contracted amounts applied to the proportion of work performed and determined through analysis with internal personnel and external service providers as to the progress or stage of completion of the services. We make significant judgements and estimates in determining the accrual balance in each reporting period. We record advance payments to CROs, CMOs or outside service providers as prepaid assets which are expensed as the contracted services are performed. As actual costs become known, we adjust our accruals. Inputs, such as the services performed, the number of patients enrolled, or the study duration, may vary from our estimates, resulting in adjustments to research and development expense in future periods. Changes in these estimates that result in material changes to our accruals could materially affect our results of operations.

Forward sale contract for Series A convertible preferred shares

In connection with the issuance of Series A convertible preferred shares on December 24, 2013, we entered into a contract for the forward sale of an additional 837,594 Series A convertible preferred shares at a price of \$5.25 per share, contingent upon certain milestones being met. This freestanding financial instrument was classified as a liability because the underlying preferred shares are contingently redeemable. The forward sale contract is carried at fair value on the balance sheet, with changes in fair value recorded in earnings. The liability was settled with the issuance of additional Series A convertible preferred shares on July 15, 2014.

We estimated the fair value of the forward sale contract for our Series A convertible preferred shares using a probability-weighted discount approach. The significant inputs used to estimate the fair value of the forward sale contract include the estimated present and future fair values of the Series A convertible preferred shares, the estimated probability of the milestone being achieved (initially 90%), the discount rate (20%) and an estimated time to the milestone event (initially estimated to be ten months).

Share/Stock-based compensation

We recognize the cost of share/stock-based awards granted to employees based on the estimated grant-date fair values of the awards. The value of the portion of the award that is ultimately expected to vest is recognized as expense ratably over the requisite service period. We recognize the compensation costs for awards that vest over several years on a straight-line basis over the vesting period. We recognize the cost of share/stock-based awards granted to nonemployees at their then-current fair values as services are performed, and are remeasured through the counterparty performance date.

Our Common B shares are issued with an applicable threshold amount set at an amount so as to qualify the shares as profits interests within the meaning of Revenue Procedure 93-27 as clarified by Revenue Procedure 2001-43. Threshold amounts are determined by the Board in good faith based on our fair market value as of the grant date. The threshold amount of profit interests granted during the year ended December 31, 2014 were between \$12.2 million and \$22.1 million. The threshold amount represents the amount which any distribution must cumulatively exceed before holders of the Common B shares participate pro rata with the holders of the Series A convertible preferred shares and Common A-1 and Common A shares in such distribution; however, holders of the Series A

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convertible preferred shares are entitled to receive their distribution priority and Common A-1 and Common A shares are each entitled to participate pro rata with the Series A convertible preferred shares until they have each received an aggregate of \$1 million, before the holders of the Common B shares would receive proceeds from any distribution.

In March 2015, upon conversion from a Delaware LLC to a Delaware corporation, we terminated the 2013 Equity Incentive Plan and adopted the 2015 Equity Incentive Plan. The outstanding Common B shares were converted into restricted common stock and options to purchase common stock with no changes to the vesting provisions. The 355,156 awards outstanding as of December 31, 2014, less subsequent forfeitures of 1,474 shares, were converted into 253,232 shares of restricted stock and 100,446 options to purchase common stock, or collectively, the Replacement Awards.

We assessed the conversion of the Common B share awards as a modification under U.S. GAAP. Because there was no change in vesting timing or conditions and there was no incremental increase in the conversion date fair value as a result of the conversion, we allocated the original Common B share values to the restricted common stock and stock options proportionate to their conversion date fair values.

We estimate the grant date fair value of the non-replacement award stock options granted under the 2015 Plan using the Black-Scholes option-pricing model, which requires the use of highly subjective assumptions to determine the fair value of the awards. These assumptions include:

- n *Expected term* The expected term represents the period that the stock-based awards are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term).
- n *Expected volatility* Since we are privately held and do not have any trading history for our common stock, the expected volatility is estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. When selecting comparable publicly traded biotechnology companies on which it has based its expected stock price volatility, we selected companies with comparable characteristics to us, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.
- n *Risk-free interest rate* The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.
- n *Expected dividend* We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

We recorded non-cash share/stock-based compensation expense granted to employees and nonemployees of \$0, \$0.1 million and \$0.8 million for the period from December 16, 2013 (inception) to December 31, 2013 and for the years ended December 31, 2014 and 2015, respectively.

We estimate our forfeiture rate based on an analysis of our actual forfeitures and will continue to evaluate the adequacy of the forfeiture rate based on actual forfeiture experience, analysis of employee turnover behavior and other factors. The cumulative impact from any forfeiture rate adjustment would be recognized in the period of adjustment and if the actual number of future

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forfeitures differs from our estimates, we might be required to record adjustments to stock-based compensation in future periods.

Valuation of equity instruments

Historically, for all periods prior to this initial public offering, the fair values of our Common B awards and the common stock underlying our stock awards were estimated on each grant date by our board of directors. In order to determine the fair value of our Common B awards and common stock, our board of directors considered, among other things, the contemporaneous valuations of our Common B shares and common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accountants Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Given the absence of a public trading market for our shares, our board of directors exercised substantial judgment and considered a number of objective and subjective factors to determine the estimated fair value of our shares, including our stage of development; progress of our research and development efforts; the rights, preferences and privileges of our convertible preferred shares relative to those of our common shares; and the lack of marketability of our common shares.

For the periods presented, the fair value of our Common B shares and common stock and other classes of shares were estimated using a market approach. There are multiple variations of the market approach. Our board of directors and the third-party valuation specialist utilized the Backsolve method, under which we and they considered the sales price of the convertible preferred shares to third-party investors and back-solved for our enterprise value.

For valuations of our shares prior to our conversion to a Delaware corporation we utilized the option pricing method, or OPM, an accepted valuation method under the AICPA Practice Guide, to allocate the enterprise value determined under the market approach to each element of our capital structure, including our common shares. The OPM values each equity class by creating a series of call options on the equity value, with exercise prices based on the liquidation preferences, participation rights and other rights. The OPM method requires significant assumptions; in particular, the time until investors in our company would experience an exit event and the volatility of our common shares. In addition, we applied a discount to the valuations due to the lack of marketability of the shares. The more significant inputs and assumptions we used in the models were our estimated equity value, the expected time until investors in our company would experience an exit event (three years), a risk-free interest rate (from 0.8% to 1.0%), the expected volatility (79% to 85%) and a discount for lack of marketability (35%).

For valuations of our common stock following our conversion to a Delaware corporation, we utilized a hybrid approach of the probability-weighted expected return method, or PWERM, and the OPM, an accepted valuation method under the AICPA Practice Guide, to allocate the enterprise value determined under the market approach to each element of our capital structure, including our common shares. The hybrid approach uses the PWERM to estimate the enterprise value under the market approach based on estimating a future value under multiple exit scenarios, going public at a high future equity value (with an early and late expected time to an exit event), going public at a low equity value (with an early and late expected time to an exit event), and remaining private with a later expected time to a liquidity event. The estimated enterprise value is then allocated to each class of equity, including common shares using the OPM or the PWERM. The PWERM was utilized in the going public scenarios and the OPM was utilized in the remaining private with a later liquidity scenario. The hybrid approach requires significant assumptions, in particular, the range of likely outcomes and their relative probability, the time until investors in our company would experience an exit event and the volatility of our common shares. In addition, we applied a discount to the valuations due to the lack of marketability of the shares.

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The following table summarizes the significant assumptions for each of the valuation scenarios used in the hybrid PWERM and OPM analysis to determine the fair value our common stock.

	Early IPO High Value	Early IPO Low Value	Later IPO High Value	Later IPO High Value	Stay Private
<u>March 15, 2015 valuation assumptions</u>					
Probability weighting	*	*	6.25%	6.25%	87.50%
Liquidity term (in years)	*	*	0.55	0.55	3.00
Discount rate	*	*	30.0%	30.0%	1.1%
Volatility	*	*	*	*	70%
Discount for lack of marketability	*	*	15.0%	15.0%	30.0%
<u>April 20, 2015 valuation assumptions</u>					
Probability weighting	3.75%	3.75%	8.75%	8.75%	75.00%
Liquidity term (in years)	0.28	0.28	0.45	0.45	2.90
Discount rate	30.0%	30.0%	30.0%	30.0%	0.8%
Volatility	*	*	*	*	70%
Discount for lack of marketability	11.5%	11.5%	14.5%	14.5%	30.0%
<u>May 25, 2015 valuation assumptions</u>					
Probability weighting	6.70%	6.70%	10.00%	10.00%	66.70%
Liquidity term (in years)	0.18	0.18	0.35	0.35	2.80
Discount rate	30.0%	30.0%	30.0%	30.0%	0.9%
Volatility	*	*	*	*	70%
Discount for lack of marketability	10.0%	10.0%	12.5%	12.5%	30.0%
<u>June 15, 2015 valuation assumptions</u>					
Probability weighting	32.00%	32.00%	8.00%	8.00%	20.00%
Liquidity term (in years)	0.13	0.13	0.29	0.29	2.75
Discount rate	30.0%	30.0%	30.0%	30.0%	1.0%
Volatility	*	*	*	*	70%
Discount for lack of marketability	7.5%	7.5%	10.0%	10.0%	30.0%

* Amount not applicable for valuation report or approach

We also utilized the probability weighted discount approach to value the forward sale contract for Series A convertible preferred shares. Inputs used to determine estimated fair value of the forward sale contract include the estimated present and future fair values of the Series A convertible preferred shares, the estimated probability of the milestone being achieved (90%), the discount rate (20%), and an estimated time to the milestone event (initially estimated to be ten months).

The dates of our contemporaneous valuations did not always coincide with the dates of our Common B share grants. For grants occurring between valuation dates, for financial reporting purposes, management estimated the fair value of the shares based on the contemporaneous third party valuations and consideration for events, progress and milestones that had occurred from the last valuation date to the date of grant.

The intrinsic value of all outstanding restricted common stock and stock options as of December 31, 2015 was \$1.2 million and \$3.6 million, respectively, based on the estimated fair value of our common shares of \$10.00 per share, the initial public offering price set forth on the cover page of this prospectus.

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In March 2016, we determined, after consultation with the underwriters, the price range set forth in our preliminary prospectus dated March 28, 2016. As of the dates of the March 10, 2015, April 1, 2015, April 22, 2015, May 28, 2015, June 15, 2015, February 26, 2016 and March 18, 2016 conversions and stock option grants, our board of directors had determined the fair value of our common stock to be \$3.47 per share (for the March 10, 2015 conversion and for the April 1, 2015 grants), \$5.04 per share (for the April 22, 2015 grants), \$6.20 per share (for the May 28, 2015 grants), \$12.81 per share (for the June 15, 2015 grants), and \$5.46 per share (for the February 26, 2016 and March 18, 2016 grants). The determination was based upon the objective and subjective factors described above. We believe the difference between the fair value of our common stock for the March 10, 2015 conversion and for the April 1, April 22, May 28, June 15, 2015, February 26, 2016 and March 18, 2016 grants, in each case as determined by our board of directors, and the then-assumed initial offering price range set forth in our preliminary prospectus dated March 28, 2016 is a result of the following factors:

- n the price range set forth in our preliminary prospectus dated March 28, 2016 necessarily assumes that the initial public offering has occurred and a public market for our common stock has been created, and therefore excludes any marketability or liquidity discount for our common stock, including those related to worsening market conditions in the fall of 2015 and early 2016, which was appropriately taken into account in our board of directors' fair value determinations;
- n differences in the valuation methodologies, assumptions and inputs used by the underwriters in their valuation analysis discussed with our management, which assume a successful initial public offering with no weighting attributed to any other outcome, compared to the valuation methodologies, assumptions and inputs used in the valuations considered by our board of directors;
- n differences in comparable companies in the life sciences and oncology markets discussed between us and the underwriters as compared to the more narrow prior analysis applied and comparable companies used by our board of directors; and
- n advancements in the development of our product candidates, in particular, the effectiveness of our investigational new drug application with the FDA in March 2016 for AEB1102 for the treatment of patients with hematological malignancies.

We have not granted any options to purchase our common stock since March 18, 2016.

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We are a biotechnology company committed to developing enzyme-based therapeutics in the field of amino acid metabolism that we believe will transform the lives of patients with inborn errors of metabolism and cancer. Our engineered human enzymes are designed to degrade specific amino acids in the blood. In inborn errors of metabolism, or IEM, a subset of rare genetic metabolic diseases, we are seeking to reduce the toxic levels of amino acids in patients. In oncology, we are seeking to reduce amino acid blood levels below the normal range where we believe we will be able to exploit the dependence of certain cancers on specific amino acids.

Our lead product candidate, AEB1102, is engineered to degrade the amino acid arginine and is being developed to treat two extremes of arginine metabolism, including arginine excess in patients with Arginase I deficiency, an IEM, as well as some cancers which have been shown to have a metabolic dependence on arginine. AEB1102 has demonstrated the ability to reduce blood arginine levels in clinical and nonclinical studies, supporting its potential use as a treatment of both Arginase I deficiency and cancer. We have an accepted investigational new drug application, or IND, with the U.S. Food and Drug Administration, or FDA, for AEB1102 for the treatment of solid tumors. In October 2015, we initiated enrollment for this dose escalation trial in patients with advanced solid tumors. We have since treated our first two cohorts of seven patients total, and a temporary reduction of blood arginine was observed, providing initial human proof of mechanism for AEB1102. We have an effective IND and plan to initiate a Phase 1 dose escalation trial in patients with hematological malignancies in the first half of 2016. We plan to initiate expansion trials in patients with solid tumors and an additional Phase 1 trial in combination with the standard of care in one or more solid tumor types in 2017. In June 2015, we submitted an IND with the FDA for AEB1102 for Arginase I deficiency. We have an effective IND for a Phase 1 dose escalation study in adult Arginase I deficiency patients and anticipate starting enrollment in the first half of 2016. We anticipate submitting a clinical trial application, or CTA, to the EMA in the second half of 2016 for a Phase 2 trial in Arginase I deficiency patients and expect to initiate that trial in the first half of 2017. We are also building a pipeline of additional product candidates targeting key amino acids and other metabolites, including homocystine, a target for another IEM as well as cysteine/cystine and methionine in oncology.

We believe amino acid metabolism is a largely unexploited area of pharmaceutical development. Amino acids are key components of metabolic processes that produce energy and enable cellular division and growth. Amino acids are also the building blocks of proteins which are critical to structural and functional elements of cells. Our goal is to engineer clinically meaningful human enzymes that act systemically on amino acids in the blood. Unlike microbial enzymes, we believe our engineered human enzymes will not be recognized as foreign by the body and will be less likely to elicit an immune response. The mechanism of action of our product candidates allows us to directly measure their activity by analyzing blood samples. We believe this approach will translate into a higher probability of clinical success for our product candidates.

We are exploring the promise of this approach through the advancement of our arginine degrading human enzyme, AEB1102. In primate studies, we have observed a substantial reduction in arginine levels after dosing with AEB1102. In our first two cohorts of seven patients total in our Phase 1 dose escalation trial in patients with advanced solid tumors, we observed a temporary reduction in blood arginine, providing initial human proof of mechanism. The target of AEB1102, arginine, provides (i) proof of mechanism for the product candidate, (ii) a direct measure of target engagement for optimization of dose and schedule, and (iii) a direct mechanistic link to efficacy in nonclinical studies. We believe AEB1102 can be applied to address both the rare IEM genetic disease, Arginase I deficiency, as well as solid tumors and hematological malignancies that depend on circulating arginine for growth and survival. AEB1102 is covered by an issued composition of matter patent that expires in 2030.

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In addition to AEB1102, we have identified several other target amino acids that we believe will have clinical relevance in the treatment of IEM and cancer. Our pipeline of engineered human enzyme product candidates in nonclinical development includes: AEB3103, an enzyme that degrades the amino acids cysteine/cystine to target a widely recognized, but previously unexploited vulnerability of cancer to oxidative stress; AEB2109, an enzyme that degrades the amino acid methionine to target methionine dependent cancers and AEB4104, an engineered human enzyme to treat another IEM by degrading the amino acid homocystine. We plan to continue nonclinical development of AEB4104, AEB3103, AEB2109 and related variants of these candidates with the aim of submitting an IND for one or more of these development candidates in late 2017. Our current product candidates have been in-licensed from the University of Texas at Austin or assigned to us from one of our founders. We retain global commercialization rights for all of our product candidates.

An integral part of our product development programs is a precision medicine strategy designed to identify patients that will benefit most from amino acid depletion therapy. For Arginase I deficiency and classical homocystinuria, widely adopted diagnostic tests are already incorporated into routine care in the form of a neonatal blood test. For oncology patients, researchers and clinical oncologists now often incorporate genetic and biomarker assessments into clinical trials and routine care with the hope of directing patients to therapies which may have a greater chance of success in treating their cancers. For AEB1102, biomarkers of tumor arginine dependence have shown value as a predictor of sensitivity to arginine depletion, and if appropriate, we plan to use those biomarkers to help us select the specific cancers to pursue in later clinical trials. We also have ongoing efforts for the identification of predictive biomarkers for the rest of the oncology pipeline. When warranted, we intend to develop companion diagnostics with the help of technology partners to aid in identifying patients whose tumors may be susceptible to amino acid depletion therapy.

We are a patient-focused organization conscious of the fact that IEM and oncology patients have limited treatment options, and we recognize that their lives and well-being are highly dependent upon our efforts and the efforts of others to develop improved therapies. For this reason, we are passionate about discovering and developing therapeutics to address IEM and oncology indications where there is a significant unmet medical need. Our goal is to create a world class company committed to efficiently developing a portfolio of product candidates to treat these diseases.

We have assembled a team with extensive experience in the discovery, development and regulatory approval of novel therapeutics. Our team has been previously involved in the development of a number of therapies approved or in development for rare metabolic genetic diseases, including Aldurazyme (laronidase), Juxtapid (lomitapide), Naglazyme (galsulfase) and PEG-PAL (pegylated recombinant phenylalanine ammonia lyase), and in oncology including Avastin (bevacizumab), Doxil (doxorubicin), Herceptin (trastuzumab), Perjeta (pertuzumab) and Rituxan (rituximab). We also leverage the expertise of our founding scientists Professor George Georgiou and Dr. Everett Stone from the University of Texas at Austin. Our investors include Lilly Ventures, Novartis Venture Fund, The Board of Regents of the University of Texas System, OrbiMed, Jennison Associates (on behalf of clients), Venrock, RA Capital Management, Rock Springs Capital and Ally Bridge Group.

Our Strategy

Our goal is to build a fully integrated biotechnology company dedicated to the development and commercialization of engineered human enzymes targeting abnormal metabolism to transform the lives of patients. To execute our strategy, we intend to:

n ***Successfully advance our lead product candidate, AEB1102, through clinical development.***

For our oncology indication we have an effective IND with the FDA for the treatment of solid tumors. In October 2015, we initiated enrollment and have since treated our first two cohorts of seven patients total in a Phase 1 dose escalation trial in patients with advanced solid tumors. We

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have an effective IND and in the first half of 2016 plan to initiate a Phase 1 dose escalation trial in patients with hematological malignancies. We plan to initiate expansion arms in patients with solid tumors and an additional Phase 1 trial in combination with the standard of care in one or more solid tumor types in 2017. If we see evidence of anti-tumor activity in the expansion phase, we plan to meet with regulatory authorities to discuss expedited regulatory strategies. For Arginase I deficiency, we have an effective IND and plan to initiate a Phase 1 dose escalation trial in the United States in up to six adult patients and, after submitting a CTA, we plan to initiate a Phase 2 trial in Europe to evaluate the safety, tolerability and dose effect on blood arginine levels in up to ten patients in the first half of 2017. If the results from the trial are supportive, we anticipate initiating a randomized Phase 3 trial in the United States and Europe. In addition, if the data from the Phase 1 trial are supportive, we may seek to accelerate our development plan for AEB1102 by requesting to use established regulatory pathways, such as Breakthrough Therapy and Fast Track designations.

n *Target enzyme-based therapeutic opportunities within IEM and oncology that have defined mechanisms of action and known disease pathways.*

Our focus is on those IEM and cancers where the biology and root causes are well understood. We believe our lead product candidate AEB1102 has a defined mechanism of action, the degradation of arginine, and is designed to reduce the elevated arginine levels caused by Arginase I deficiency. Similarly, the dependence of various cancers on arginine is well understood and documented in the scientific and medical literature. We believe that developing product candidates that directly impact known disease pathways will increase the probability of success of our development programs.

n *Develop a precision medicine strategy that increases the probability of clinical success.*

An integral part of our product development programs is a precision medicine strategy designed to identify patients that will benefit most from amino acid depletion therapy. In the United States, we are taking advantage of the identification of patients with Arginase I deficiency through a widely adopted diagnostic test that has been incorporated into routine care in the form of a neonatal blood test since 2006. In oncology, we are exploring the predictive value of candidate biomarkers to identify patients with tumors sensitive to amino acid deprivation. We believe that enrolling these patients in our clinical trials may lead to potential proof-of-concept earlier in clinical development and may have a greater chance of success of treating their cancers effectively. When warranted, we intend to facilitate the development of companion diagnostics with the help of technology partners to aid in identifying patients whose tumors may be susceptible to amino acid depletion therapy.

n *Concurrently develop and commercialize multiple product candidates.*

Development of multiple engineered human enzyme therapeutics generates organizational efficiencies and economies of scale. As a result, we believe we can concurrently develop several clinical-stage product candidates, resulting in a more diversified portfolio that provides multiple opportunities to create value. In addition, we intend to build our own research organization to provide in-house drug discovery capabilities, and to continue to leverage our relationships with the University of Texas at Austin and other academic institutions to expand our portfolio of product candidates.

n *Seek global approval and commercialization of our product candidates.*

We retain worldwide intellectual property rights for all of our product candidates. We will pursue clinical and regulatory programs for approval in the United States and internationally. Our plan is to establish a focused commercial organization in the United States and strategically evaluate partnership opportunities internationally.

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Our Focus Abnormal Amino Acid Metabolism

Our company was founded to develop therapeutics for diseases characterized by abnormal amino acid metabolism. Metabolism refers to fundamental chemical reactions that are critical to life-sustaining processes. Metabolism follows specific pathways that are comprised of various biochemical reactions generally catalyzed by proteins known as enzymes. Enzymes accelerate complex reactions and serve as key regulators of metabolic pathways by responding to changes in the cell's environment or signals from other cells.

An in-depth understanding of abnormal metabolic pathways is crucial to developing therapies that may address various disease states, including IEM and cancer. Our core capability of exploiting the metabolic pathways of IEM diseases has allowed us to develop engineered human enzyme therapies with the potential to reduce toxic levels of amino acids that may lead to novel, disease-modifying treatments for these rare diseases. In addition, with our focus on the innovative field of cancer cell metabolism, we strive to leverage our engineered human enzyme product candidates to degrade the key nutrients that promote cancer cell survival and proliferation.

Background on inborn errors of metabolism

Enzymatic defects in metabolic processes contribute to a class of genetic diseases known as IEM. These are a broad group of more than hundreds of rare metabolic genetic diseases where the defect in a single metabolic enzyme disrupts the normal functioning of a metabolic pathway. These defects lead either to abnormal accumulation of upstream metabolites that may be toxic or interfere with normal function, or to a reduced ability to synthesize essential downstream metabolites.

Most of these diseases often have severe or life-threatening characteristics. The incidence of a single IEM often occurs in fewer than one per 100,000 live births. Many IEM are likely to be under-diagnosed. Current treatment options for many of these disorders are limited. Diet modification or nutrient supplementation can be beneficial in some IEM. Several of these disorders have been treated successfully with enzyme therapy. Some examples of this type of therapy for an IEM include Naglazyme (galsulfase) as a treatment for MPS 6 (mucopolysaccharidosis VI), or Fabrazyme (agalsidase beta) as an enzyme replacement therapy for patients with Fabry disease (alpha-galactosidase A deficiency).

Our focus is on those IEM that are characterized by excess levels of amino acids and other metabolites that become toxic to patients. In these circumstances, we expect patients to benefit from reduced levels of the target amino acid or metabolite to a normal concentration range. We believe this can be successfully achieved through our enzyme replacement therapy. We are targeting a urea cycle disorder, Arginase I deficiency, for our lead product candidate, AEB1102. This cycle has the principle function of detoxifying ammonia, a normal byproduct of amino acid metabolism. Arginase I reduces arginine levels, and is the final step of the urea cycle, releasing urea for secretion by the kidney.

We are developing AEB1102 to serve as an effective enzyme replacement therapy for patients with Arginase I deficiency, which leads to elevated levels of arginine in blood. While a protein restricted diet is part of the treatment regimen for Arginase I deficiency, it is not effective in normalizing blood arginine due to the body's continued production and processing of ammonia that results in continued production of arginine. Symptoms resulting from defects in the urea cycle metabolic pathway, such as increased levels of ammonia, have been the successful target of other drug development efforts including RAVICTI (glycerol phenylbutyrate) and BUPHENYL (sodium benzoate) which help to remove ammonia. Despite the acceptance of these drugs, they do not treat the underlying cause of the disease. We believe that AEB1102 represents a potential therapeutic candidate to treat the excess levels of arginine resulting from Arginase I deficiency.

Table of Contents***Cancer background***

Cancer is the second-leading cause of death in the United States. The American Cancer Society estimates that in 2015 there will be approximately 1.7 million new cases and approximately 589,000 deaths from cancer in the United States. Cancer originates from defects in the cell's genetic code, or DNA, that disrupt the mechanisms that normally prevent uncontrolled cell growth.

The most common methods of treating patients with cancer include surgery, radiation and drug therapy, including biological products. A cancer patient often receives treatment with a combination of these modalities. Surgery and radiation therapy are particularly effective in patients in whom the disease is localized. Physicians generally use systemic drug therapies in situations in which the cancer has spread beyond the primary site or cannot otherwise be treated through surgery. The goal of drug therapy is to damage and kill cancer cells or to interfere with the molecular and cellular processes that control the development, growth and survival of cancer cells. In many cases, drug therapy entails the administration of several different drugs in combination. Over the past several decades, drug therapy has evolved from relatively non-specific chemotherapeutic drugs that kill both healthy and cancerous cells, to targeted therapies more specific to molecular pathways involved in the cancer.

Emerging areas in cancer therapy

Beyond chemotherapeutics and targeted drug therapies, several new approaches to the development of novel cancer treatments are underway. These approaches include, but are not limited to treatment with drugs or other methods that stimulate the immune system to attack cancer cells, antibody drug conjugates that carry a powerful chemotherapy payload that is only released into targeted cancer cells, drugs that target the changes in gene activity that occur in cancer cells and drugs that target oncogenic drivers in patients with tumor types that harbor genetically similar alterations.

We believe that the altered metabolism of cancer cells—the atypical uptake and break down of nutrients—also provides an opportunity to develop important new cancer treatments. Cancer cells rapidly change how they take-up and utilize nutrients. These adaptations fuel tumor growth and protect cancer cells from the damage caused by reactive oxygen species, or ROS, and various immune system responses. However, while cancer cell metabolic abnormalities fuel tumor growth, they also expose vulnerabilities that can be targeted to selectively destroy tumor cells. It is our belief that depriving cancer cells of key amino acids that are essential for cell survival and tumor growth will provide an effective treatment for some cancers. While the dependence of different cancers on specific amino acids has been known for many years, it has not been widely exploited in the clinical setting.

Enzyme-based therapies that degrade amino acids have shown clinical benefit in the treatment of cancer. However, some microbial-derived enzymes present limitations. For example, Oncaspar (pegaspargase) and Erwinaze (Erwinia chrysanthemi) were approved as part of a multi-agent chemotherapeutic regimen for the treatment of patients with acute lymphoblastic leukemia. Degrading the amino acid asparagine with an *E. coli*-derived enzyme, Oncaspar (pegaspargase) in combination with chemotherapy generates much improved remission rates as compared to chemotherapy alone. As reported in the scientific and clinical research literature, Oncaspar (pegaspargase) alone achieved complete remission rates of up to 60%; however the duration of remission is relatively short. In combination with chemotherapy, overall survival rates approach 90%. However, in some patients this regimen is poorly tolerated. In addition, tumor arginine dependence has been reported in the scientific and medical literature to result in responses to a microbial-derived arginine-degrading enzyme in patients in trials with acute myelogenous leukemia, mesothelioma, hepatocellular carcinoma and melanoma. However, despite the reported clinical impact, the microbial arginine degrading enzyme elicited an immune response that neutralizes the activity of the drug and therefore may have limited clinical utility.

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The use of microbial enzymes as therapeutics is often limited by an immune response to a foreign protein. We expect our enzyme product candidates, which are engineered from human proteins, will be less likely to elicit an immune response as compared to microbial enzymes. We believe our technology should provide greater flexibility with respect to the target amino acids that can be addressed. Our portfolio of candidate enzyme therapies currently targets key amino acids, including arginine, cysteine/cystine and methionine that are nutrients necessary for tumor cell survival and proliferation in some malignancies.

By depriving cancer cells of these amino acids via our engineered human enzyme product candidates, we provide a novel approach that, when used alone or in combination with existing or emerging standards of care, has the potential to be an effective treatment paradigm for cancer patients. Published literature suggests that a variety of cancers could potentially respond to amino acid deprivation resulting from enzyme therapies, which offers us many potential targets for cancer treatment opportunities.

The Aeglea Approach

We believe our approach to drug discovery and development will lead to transformative therapies for patients. We apply our cellular metabolism expertise to build a portfolio of engineered human enzyme therapeutics that target distinct metabolites and provide additional therapeutic options for IEM and cancer. We expect that conducting clinical trials with a targeted agent in the appropriate patient population has the potential to lead to expedited regulatory development. We plan to partner closely with worldwide regulatory authorities and to utilize all available regulatory tools such as orphan, fast track and breakthrough designations, as well as accelerated approval as appropriate.

Target selection. We identify new targets for enzyme therapeutics by leveraging scientific and medical literature and available clinical precedents. For our IEM portfolio, we focus on diseases that are caused by a mutation in a single metabolic enzyme and where the biology and root causes are well understood. We believe that developing drugs that directly impact known disease pathways will increase the probability of success of our development programs. For our oncology portfolio, we focus on different tumors that are dependent on specific amino acids for survival. We believe these known targets require human enzymes with improved properties to be developed into an effective and well-tolerated therapeutic. In addition, the potential for other amino acid targets is still emerging, and will require additional research to evaluate the potential therapeutic opportunity.

Product candidate identification. Once a potential therapeutic target is identified, we employ molecular modeling to evaluate human enzyme candidates with the potential to be developed into therapeutics with the requisite pharmacological properties. We conduct a detailed analysis of the structural biology of the target metabolic enzyme and the entire pathway of interest to determine the scientific feasibility of the native human enzyme as a scaffold for engineering and optimization.

Once a native human enzyme has been identified as a promising product candidate, we modify the molecule by using protein engineering techniques to create enzymes displaying the requisite catalytic and pharmacological properties that can degrade these targets and effectively address the metabolic defects observed in IEM or the dependence of certain cancers on amino acids or other metabolites. Certain metabolites require modified enzymes to properly control their levels in a therapeutic setting. We screen libraries of enzyme variants with high-capacity testing techniques tailored to identify the mutations that we believe will have the most therapeutic potential. Multiple rounds of mutagenesis and screening may be employed iteratively to obtain the desired enzyme activity. We engineer human proteins as scaffolds to develop therapeutic products and to help avoid the immunogenicity problems seen with non-human protein-based drugs. Our goal is to create engineered human enzymes with the appropriate properties to be developed into effective and well-tolerated therapeutics.

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Once we identify a lead enzyme, we then engage third parties to manufacture sufficient quantities for nonclinical studies. These *in vivo* studies test for drug-like properties, measuring the pharmacodynamics and pharmacokinetics after administration in an animal model. We believe this provides us with a preliminary understanding of dosing requirements for testing of both efficacy in animal models of human disease, and safety in toxicology studies.

Clinical trial and regulatory execution. An integral part of our product development programs is a precision medicine strategy designed to identify patients that will benefit most from amino acid depletion therapy. Enriching our clinical trials with these patients will potentially lead to proof of concept earlier in clinical development. In the United States, we are taking advantage of a widely adopted neonatal diagnostic blood test that has been incorporated into routine care to identify patients with Arginase I deficiency since 2006. In oncology, we are using patient tumor samples to determine which types of cancers express biomarkers of predicted arginine dependence. If we see early evidence of a product candidate's clinical activity, we plan to meet with regulatory authorities to discuss expedited regulatory strategies. We are also seeking additional product candidates with the potential for efficient biomarker assisted development programs similar to our approach for AEB1102, and have ongoing efforts towards the identification of predictive biomarkers for our oncology pipeline. Where appropriate we intend to develop companion diagnostics, with the help of technology partners, to identify patients whose tumors may be susceptible to amino acid depletion therapy.

Our Development Programs

The following table summarizes our development programs:

AEB1102

AEB1102 is human Arginase I, engineered to reduce arginine levels to treat both patients with Arginase I deficiency and patients with arginine-dependent solid tumors and hematological malignancies. For our oncology indication we have an effective IND with the FDA for the treatment of

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solid tumors. In October 2015, we initiated enrollment and have since treated our first two cohorts of seven patients total in a Phase 1 dose escalation trial in patients with advanced solid tumors. We have an effective IND and plan to initiate a Phase 1 dose escalation trial in patients with hematological malignancies after investigating the optimal biological dose in solid tumors in the first half of 2016. We plan to initiate expansion arms in solid tumors and an additional Phase 1 trial in combination with the standard of care in one or more solid tumor types in 2017. If we see evidence of anti-tumor activity in the expansion phase, we plan to meet with regulatory authorities to discuss expedited regulatory strategies. In June 2015, we submitted an IND for AEB1102 for Arginase I deficiency. Following discussion with the FDA, we withdrew our submitted IND in order to comply with new draft guidance issued by the FDA on nonclinical assessment of enzyme replacement therapies. In October 2015, we met with the FDA and the MHRA in the United Kingdom regarding our planned clinical and regulatory path for AEB1102 in Arginase I deficiency. Based on these discussions, we submitted a revised IND, which became effective in January 2016, and plan to submit a CTA to the EMA and initiate clinical trials in patients with Arginase I deficiency in 2016 in the United States and in the first half of 2017 in Europe.

We believe our lead compound offers the following advantages:

- n *Market opportunities in both IEM and oncology.* We believe that AEB1102 can be applied to address both the rare IEM Arginase I deficiency, as well as solid tumors and hematological malignancies that depend on arginine for growth and survival.
- n *Well-understood mechanism of action.* Arginase I has been investigated extensively in both scientific and clinical research as a method for degrading arginine, a naturally occurring amino acid that is one of the building blocks of proteins and is a contributor to cell proliferation and survival. AEB1102 has demonstrated the ability to reduce blood arginine levels in our nonclinical studies. In addition, in the first two cohorts of seven patients total in our Phase 1 dose escalation trial in patients with advanced solid tumors, we have observed a temporary reduction in blood arginine levels.
- n *Proof of mechanism.* The target of AEB1102, the amino acid arginine, is easily measured and detected in the blood to enable selection of the optimal dose and schedule.
- n *Clinical precedent for our approach in oncology.* Third-party clinical trials with a microbial arginine degrading enzyme have yielded positive results in acute myelogenous leukemia, metastatic melanoma, hepatocellular carcinoma and pleural mesothelioma. These clinical trials highlight the potential of targeting the metabolic dependence of some cancers on arginine as an attractive approach for cancer treatment.
- n *Improved activity and stability.* AEB1102 has increased catalytic activity and serum stability compared to native human Arginase I, due to the substitution of the native manganese cofactor with cobalt. A cofactor is a non-protein chemical compound required for an enzyme's biological activity. Pegylation further improves the half-life *in vivo*. These improvements have provided increased potency in both our *in vitro* and *in vivo* models.
- n *Potential of lower risk of immunogenicity.* The AEB1102 amino acid sequence is engineered from the native human amino acid sequence. As such, we believe that patients' immune systems are less likely to recognize this therapeutic candidate as a foreign molecule and mount an immune response as compared to microbial enzymes.
- n *Manufacturing.* We have entered into a strategic partnership with an experienced manufacturer and have agreements with other manufacturers in the field of biologic drugs. We have produced AEB1102 in *E. coli* for our planned clinical trials.
- n *Intellectual property.* We have an issued composition of matter patent covering AEB1102 that expires in 2030, with the potential for patent-term extension. Intellectual property rights to AEB1102 were assigned to us on an exclusive and royalty-free basis.

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AEB1102 background, preliminary clinical data

AEB1102 is being evaluated in an ongoing, open-label, multiple dose, dose-escalation trial to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of AEB1102 in patients with advanced solid tumors who have failed standard therapies for their diseases. This Phase 1 trial was initiated in October 2015. As of February 16, 2016, the cutoff date for the most recent preliminary data analysis, we have treated two cohorts of seven patients in total. As shown in the following chart, a temporary reduction in blood arginine was observed:

Blood Arginine Levels Observed in First Two Cohorts After Treatment with AEB1102

The data presented are preliminary and unaudited, and are subject to change. While we believe these data provide initial human proof of mechanism for AEB1102, these data may not necessarily be predictive of the final results of all patients intended to be enrolled in this Phase 1 trial or in future trials. Given the nature of the patient population enrolled in this trial, we expect to and have observed serious adverse events in some of these patients, including death. Six serious adverse events were reported in a total of four patients. These included hypercalcemia, bacteremia, pericardial effusion, respiratory failure and worsening of the patients' underlying cancer, none of which were assessed as trial therapy-related. All patients recovered except for one who died after discontinuing the trial due to worsening of the underlying cancer. To date, we do not consider any of these serious adverse events to be drug-related and are proceeding with the dosing schedule.

AEB1102 background, nonclinical results

Arginase I has been investigated extensively as a method for reducing arginine levels. Native human Arginase I, however, is not an ideal therapeutic candidate due to low catalytic activity and poor stability under physiological conditions.

We are developing a therapeutic candidate using native human Arginase I and modifying it by substituting cobalt for the manganese cofactor, which increases catalytic activity and serum stability. We also improve the half-life *in vivo* by pegylation, or chemically adding polyethylene glycol to the molecular structure, of the modified enzyme. To support its development as a product candidate, we have improved on the catalytic activity and stability of human Arginase I, providing increased potency in both *in vitro* and *in vivo* models.

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AEB1102 and its precursors have shown improved serum stability and catalytic activity when compared to native human Arginase I. The following chart illustrates the improved serum stability in an *in vitro* study as measured by half-life with an earlier version of cobalt-substituted pegylated human Arginase I, which is a precursor of AEB1102:

That same study also showed a ten-fold increase in catalytic activity. In a separate study conducted by our strategic manufacturing partner, AEB1102 showed improved catalytic activity approximately 20-times greater than pegylated native human Arginase I in an *in vitro* arginine degradation assay:

In an *in vivo* animal study, we administered a single intravenous dose of either AEB1102 or the native human Arginase I to cynomolgus monkeys, and we measured blood arginine levels over time. Whereas the native enzyme caused a transient reduction in blood arginine over 24 hours, AEB1102 at

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the same dose reduced the arginine concentration to below the limit of detection for approximately one week (160 hours). Our experiment showed a more favorable pharmacodynamics profile of AEB1102 over the native human enzyme.

We have also completed a dose-range finding study in cynomolgus monkeys, which utilized pharmacokinetic, blood levels of drug activity, and pharmacodynamic, blood arginine levels, as endpoints to identify active drug levels. The pharmacokinetic and pharmacodynamic attributes of AEB1102, as shown in this study, suggest a once per week clinical regimen for oncology. Gastrointestinal and hematologic adverse events were seen predominately at high doses in toxicology studies in the cynomolgus monkey. This study has also served as a guide for the execution of our IND-enabling toxicology programs, in which a No Observed Adverse Effect Level was identified. The toxicology studies also enabled determination of the starting dose for our future human clinical trials for patients ages 18 years and older. Additionally, we have completed the live-animal portion of a juvenile rat toxicology study, which we believe will ultimately support treating patients age two years and older in both IEM and oncology in the United States.

Arginase I deficiency background

Arginase I deficiency is a rare genetic disorder caused by a mutation in the Arginase I gene, ARG1, which leads to the inability to degrade arginine levels. Patients with this disease are predisposed to neurologic symptoms including cognitive deficits and seizures and frequently suffer from spasticity, loss of ambulation, and severe intellectual disability.

Arginase I deficiency is a urea cycle disorder, with a reported incidence of 1:350,000 to 1:1,000,000 live births. It is believed that approximately 500-600 individuals in the United States and Europe suffer from Arginase I deficiency. Although Arginase I deficiency is a rare disease, we believe our working relationships with the Urea Cycle Disorders Consortium and the National Urea Cycle Disorders Foundation patient advocacy group will assist in our enrollment of candidates for our clinical trials. Through these relationships, we have identified an aggregate of approximately 20 patients with Arginase I deficiency in the United States and approximately 16 patients in Europe to date. Because neonatal blood testing for this disorder did not become common in the United States until 2006, we

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believe that approximately half of those individuals identified in the United States are younger than 18, and thus would not be eligible for inclusion in our proposed Phase 1 trial in the United States. The onset of symptoms typically occurs between one and three years of age and diagnosis in the United States most often occurs through newborn blood screening for this disease, which takes place in 49 U.S. states. Because the symptoms of Arginase I deficiency are similar to a number of other ailments, including cerebral palsy, we believe the exact incidence and prevalence of Arginase I deficiency are likely underestimated in regions such as Europe that do not mandate newborn blood screening for this disease.

There is no approved therapeutic agent that addresses the cause of Arginase I deficiency, although the medical literature suggests that disease progression can be slowed with strict adherence to dietary protein restriction. Dietary modification, which requires the use of specially formulated supplements, can reduce plasma arginine levels. This therapy is inadequate for treating the majority of patients with Arginase I deficiency, is difficult to manage, is poorly tolerated and is expensive. Therapy with the ammonia scavenging drugs RAVICTI (glycerol phenylbutyrate) or BUPHENYL (sodium benzoate) can be used to reduce elevated ammonia levels but does not appear to affect circulating arginine. Liver transplantation has been reported to be effective in patients to achieve normalization of arginine levels, but despite these successes, this intervention is available to only a small fraction of patients and carries a significant risk of mortality and morbidity.

The lack of treatment options that directly address the cause of Arginase I deficiency points to the need for a therapy that will lower arginine levels to within the normal range and promote the lifelong maintenance of normal arginine levels. The development of such a therapeutic and its initiation early in life could potentially minimize the exposure to the neurotoxic effects of arginine and its metabolites, and offer the potential for normal neurocognitive development in these patients.

AEB1102 clinical development in Arginase I deficiency

AEB1102 is intended to replace the function of Arginase I in patients, and return the elevated arginine levels to the normal physiological range. Normalization of arginine levels is anticipated to slow or halt the progression of disease in these patients. In two mouse genetic models of neonatal and adult Arginase I deficiency, AEB1102 was shown to be effective in lowering blood arginine. Also, as illustrated in the figure below, we conducted a nonclinical study in rats in which hyperargininemia was induced, whereby we observed decreases in blood arginine to normal levels for approximately 48 to 72 hours following dosing.

Blood Arginine Levels in Hyperargininemic Rats after Dosing

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We have obtained orphan drug designation in the United States for AEB1102 for the treatment of patients with Arginase I deficiency. The FDA may grant orphan drug designation for drugs or biologics designed to treat disorders affecting fewer than 200,000 people in the United States. In October of 2015, we met with the FDA and the MHRA to discuss a potential Phase 1 dose-escalation trial and Phase 2 trial, respectively. We have an effective IND and, in the first half of 2016, we plan to initiate an open-label Phase 1 dose-escalation trial in the United States in patients 18 years of age and older to evaluate pharmacokinetics and pharmacodynamics in up to six patients with Arginase I deficiency. If the data from the Phase 1 trial are supportive, we may seek to accelerate our development plan for AEB1102 by requesting to use established regulatory pathways, such as Breakthrough Therapy and Fast Track designations. For our planned Phase 2 trial in Europe, based on discussions with the MHRA, to support dosing patients ages two and older with AEB1102 for the full duration of the Phase 2 trial in Europe, we will submit a total of six months of nonclinical toxicology data. We plan to initiate this Phase 2 trial in Europe in the first half of 2017 to evaluate the safety, tolerability, dose and efficacy of intravenous administration of AEB1102 in up to ten patients with Arginase I deficiency, starting enrollment initially at age 12 and older. This Phase 2 trial is intended to begin with a four-week observation period, followed by a dose escalation for approximately 12 weeks, or until arginine is normalized. We also intend to measure signs and symptoms of the disorder, including a quality-of-life assessment and neurocognitive measurements. If the data are favorable, patients in the Phase 2 trial will be eligible for a long-term extension study. We expect to complete enrollment of this trial in 2018. If the results from the trial are supportive, we anticipate initiating a randomized Phase 3 trial enrolling approximately 15-30 patients that if successful will support a BLA filing with the FDA and a MAA with the EMA.

We have met with the FDA on two occasions regarding the pathway for potential approval of AEB1102 for the treatment of Arginase I deficiency. Although the FDA recommended in our 2014 Pre-IND meeting that we measure age appropriate neurocognitive outcomes in our trials for marketing approval under the regular approval pathway, the FDA has agreed that the primary endpoint of our Phase 2 and Phase 3 trials could be the normalization of blood arginine levels; provided that we can provide adequate justification that normalization of plasma arginine in the target population is reasonably likely to predict clinical benefit. To do this, we believe the FDA expects some evidence of consistent trends in the stabilization or improvement of clinical signs and symptoms of Arginase I deficiency to be observed in the Phase 3 trial to support the primary endpoint. The FDA has suggested that we investigate multiple endpoints that can show a clinically meaningful benefit, such as neurocognitive outcomes and quality-of-life measurements, and not necessarily focus on achieving a statistically significant result (usually measured by a statistical value that indicates the likelihood that the result is not due to chance) on a single clinical endpoint, given the small number of patients expected to be enrolled in this trial. The FDA stated that the Phase 3 trial length and design will need to be adequate to assess safety in the target population, stated that it is not clear that the time needed to show an effect on a biomarker will be an adequate duration to characterize safety and recommended that we reach agreement with the FDA on the duration of such a trial if we decide to pursue an accelerated approval development plan. Finally, if we obtain accelerated approval, we will be required to conduct a post-approval controlled trial that verifies clinical benefit in neurocognitive outcomes, and the FDA has stated that it expects the verification study to be underway at the time of accelerated approval. With respect to Arginase I deficiency, we do not expect to need FDA regulatory approval of any diagnostic test prior to obtaining approval, if any, of AEB1102 for that indication. A diagnostic test for Arginase I deficiency already exists in the form of a widely adopted neonatal blood test that is a part of mandatory newborn screening in 49 U.S. states and incorporated into routine care for diagnosis and treatment of patients with Arginase I deficiency.

Table of Contents***AEB1102 background in oncology***

We are planning to target the dependence of some cancers on the amino acid arginine using AEB1102. Arginine is considered a semi-essential amino acid since in some circumstances cells cannot make sufficient amounts of arginine. These circumstances include conditions of enhanced proliferation, tissue injury or stress. The role of arginine and its metabolites in cancer has been studied extensively in nonclinical models with demonstrated effects, including enhancement of tumor growth and cellular proliferation. Conversely, restriction of dietary arginine attenuates tumor growth and metastasis in experimental tumor models.

Many types of cancers lose the ability to synthesize intracellular arginine, principally due to deficiency in the expression of any one or more of the following enzymes: ornithine transcarbamoylase, or OTC, argininosuccinate synthase, or ASS and argininosuccinate lyase, or ASL. As a result, these cancers depend on extracellular arginine uptake. When deprived of this tumor-essential nutrient, cancer cells die, establishing a correlation between their inability to synthesize arginine and vulnerability to arginine deprivation. As set forth in the figure below, based on data from our nonclinical studies and the published scientific and medical literature, Arginase I degrades arginine to ornithine and urea. Ornithine cannot be used to make arginine by any cancer cells that lack expression of OTC, ASS or ASL.

As documented in scientific and medical literature and from our own nonclinical research, the lack of expression of any one or more of the enzymes OTC, ASS or ASL in tumor cells has been shown to be a predictive biomarker for arginine dependent cancer cells. The chart below summarizes data from human tumor sample studies from published scientific and medical literature. Each solid bar identifies the tumor type and the percent of tumors that were found to have one or more of the biomarkers predicting arginine dependence. The number of different patient tumor samples tested is displayed in the column on the right. These results suggest that the vulnerability to arginine deprivation may be predicted in a range of tumor types. Further, a separate study reported in the scientific and medical literature with 27 metastatic melanoma patients treated with a microbial arginine degrading enzyme, the lack of expression of ASS predicted improved clinical outcome for the patients.

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Clinical development plan for AEB1102 in oncology

With an effective IND for AEB1102 for the treatment of solid tumors we initiated enrollment and treated our first two cohorts of seven patients total in a Phase 1 trial in solid tumors with two stages: dose escalation and expansion. The primary objectives of the dose escalation stage are to determine the optimal biological dose, which will be based on changes in the target, blood arginine, as well as to determine the safety, tolerability and pharmacokinetic profile of AEB1102. The inclusion criteria include patients with advanced solid tumors who have failed standard treatment for their disease. This includes adult patients with tumors that are locally advanced or metastatic that have progressed, have been nonresponsive to available therapies or for which no standard or available therapy exists. We expect that between 24-48 patients will be enrolled in the dose-escalation portion of the trial, depending on the number of dose levels studied and the adverse effects observed. We have an effective IND and intend to initiate an additional Phase 1 trial for hematological malignancies in the first half of 2016. We expect that up to 48 patients will be enrolled in the dose escalation portion of this trial and an additional ten patients will be enrolled at the maximum tolerated dose level to further evaluate safety at this dose level. At the end of our Phase 1 dose escalation in solid tumors, we intend to initiate expansion arms in different tumor types, which we have yet to determine. We anticipate up to 60-75 patients may be enrolled in these three expansion arms. The primary objective of the expansion phase is to assess safety and preliminary evidence of antitumor activity across multiple tumor types. An additional Phase 1 expansion trial will evaluate AEB1102 in combination with a standard of care in one or more solid tumor types.

The selection of the solid tumor types for the Phase 1 expansion arms arises from our biomarker strategy, which is composed of two parts. First, we plan to confirm and extend the published scientific literature on the biomarkers of arginine dependence in multiple tumor types as shown in the chart above. Based on those data, we plan to further assess the predictive value of the biomarkers in patient-derived xenograft models, which are based on testing drug activity in patient tumor fragments. The results of these experiments, along with the results from our dose-escalation stage, will inform the choice of specific cancer indications for our expansion arms. If we use a biomarker-based test to

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identify and only enroll patients in clinical trials with tumors that express the biomarker, we expect the FDA will require the development and regulatory approval of a companion diagnostic assay as a condition to approval of the product candidate for that indication.

Targeting cysteine/cystine and oxidative stress for oncology

Reactive oxygen species, or ROS, have been widely reported in the scientific and clinical research literature to have enhanced production in tumors creating oxidative stress, resulting in damage to lipids, membranes, structural and functional proteins and DNA. Major sources of oxidative stress in cancer include: metabolic activities due to aberrant growth-promoting pathways, infiltrating inflammatory cells, as well as standards of care such as chemotherapy and radiation therapy. Glutathione is a key natural protector of ROS-mediated damage and has an enhanced role in protecting tumor cells from high levels of ROS. To survive in this hostile environment, cancer cells produce high levels of glutathione which preferentially reacts with and neutralizes the otherwise damaging ROS. Glutathione cannot be transported into cells from outside the cell, and must be synthesized in each cell. In order to satisfy the tumor's demand for glutathione, an adequate supply of cysteine/cystine is required. Reducing available cysteine/cystine from outside the cell decreases the levels of glutathione, increasing ROS-related damage to cancer cells and triggering cancer cell death.

The production of ROS is both an initiator as well as a promoter of cancer, requiring increased production of glutathione for cancer survival. However, many cancer treatments are also cytotoxic through the production of ROS. This apparent paradox is receiving increased attention as a potential tumor vulnerability, and underlies the mechanistic rationale for selective tumor killing by using a therapeutic enzyme to reduce available cysteine/cystine in the blood. While chemotherapy and radiation therapies are often highly efficient at eliminating the bulk of cancer cells, treatment resistant cancer stem cells are highly resistant to ROS mediated damage and survive anti-cancer therapy. These cancer stem cells are thought to be a cause of patient relapse.

Cancer stem cells are protected from ROS stress through increased glutathione production in both hematological malignancies and solid tumors. Based on an extensive body of evidence from the scientific and clinical research literature, we believe targeting the glutathione dependence of cancer will not only have direct anti-tumor activity but may also show synergy in combination with standards of care, depleting the cancer stem cells to provide a prolonged benefit to patients.

AEB3103

AEB3103, our lead enzyme in this program, is an engineered human enzyme that targets the degradation of the amino acid cysteine/cystine. To date, no native human cysteine or cystine degrading enzyme has been identified. Initial efficacy testing demonstrated significant depletion of glutathione and significantly increased levels of ROS in HMVP2 prostate cancer cells. As shown below, *in vivo* AEB3103 demonstrated significant inhibition of growth against this mouse allograft prostate cancer model. Treatment appeared to be well tolerated as animals showed no change in appetite or weight loss. This is expected since normal cells have the ability to synthesize cysteine and thus maintain their ROS-protective ability even upon depletion of extracellular cysteine/cystine. Also shown below are additional studies of AEB3103, which demonstrate that AEB3103 had a significant effect inhibiting tumor growth in the mouse MDA-MB-23 xenograft model of triple negative breast cancer (tumors lacking the estrogen receptor, progesterone receptor, and high expression of the HER2 gene). This type of cancer has been described in the scientific and medical literature as being highly resistant to chemotherapy and oxidative stress and represents potential clinical indication for AEB3103 development. Hematological malignancies such as acute myeloid leukemia, chronic lymphocytic leukemia, and multiple myeloma have also been described in the scientific and medical literature as having a critical dependence on glutathione for growth and survival. We believe AEB3103 provides us with the

opportunity to exploit a vulnerability of cancer that has been recognized for over 60 years, but

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not yet exploited for therapeutic benefit. We plan to continue our nonclinical development efforts for AEB3103 through 2016 and, if appropriate, proceed to IND-enabling studies with a development candidate from this program in 2017.

Targeting methionine dependence for oncology

The dependence of tumors on the essential amino acid methionine for survival has been described extensively, with the demand of some tumors for methionine far exceeding that of normal tissues. This dependence has been exploited in the clinic as a diagnostic where an analog of methionine is the preferred contrast agent for imaging of glioblastomas, astrocytomas and melanoma metastases to the brain. Methionine supports five metabolic pathways which promote tumor growth, protecting tumor cells from a hostile environment, and ultimately form the basis for selective tumor killing based on

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methionine starvation. Over 40 years of research on tumor methionine dependence has been built on the use of a bacterial methionine degrading enzyme. This microbial enzyme never advanced in clinical development, but provided a strong rationale for targeting methionine dependence in tumors.

The finding of tumor methionine dependence led to efforts to attempt dietary manipulation as an anti-cancer therapy. These efforts provided evidence of limited activity, but did not reduce methionine levels sufficiently. Enzyme mediated methionine depletion in animals results in far lower serum levels than nutritional restriction can achieve, suggesting that our therapeutic approach with an engineered human methionine-degrading enzyme is likely to achieve meaningfully improved efficacy in combination with standard of care.

Because there are specific metabolic pathways dependent on methionine metabolism, we believe methionine depletion used in combination with a variety of chemotherapeutics will be complementary to enzyme-mediated methionine depletion in blood, and may result in synergistic effects. We anticipate new treatment paradigms utilizing this approach, if successfully developed and approved, will have a significant impact with both improved patient responses and long term outcomes.

AEB2109

AEB2109, our lead enzyme in this program, is an engineered human enzyme that targets the degradation of the amino acid methionine. To date, no native human methionine degrading enzyme has been identified. Earlier work from our enzyme engineering program has been presented in the scientific literature describing activity in an animal tumor model. We believe AEB2109 provides us with the opportunity to exploit a tumor vulnerability that has been recognized for over 40 years, but not yet exploited for therapeutic benefit. We plan to continue our nonclinical development efforts for AEB2109 through 2016 and, if appropriate, proceed to IND-enabling studies with a development candidate from this program in 2017.

AEB4104 and additional pipeline opportunities

Our ongoing research efforts have identified various opportunities to leverage our expertise in the field of enzyme biochemistry to develop product candidates targeting various IEM and tumor metabolism mechanisms. We are currently in the early discovery stages for an engineered human enzyme therapy with AEB4104, the most advanced enzyme in that program, targeting the reduction of elevated levels of the amino acid homocystine. Elevated blood levels of this amino acid arise in the IEM called classical homocystinuria. We plan on demonstrating activity for AEB4104 or a related candidate in a model of this IEM by the second half of 2016. We believe that classical homocystinuria represents a viable market opportunity and significant unmet medical need, which we plan to address by continuing our development of AEB4104 and related enzymes. Regarding oncology indications, we will continue to explore other amino acids for targeted enzyme treatments in combination with emerging and current standards of care such as chemotherapy and radiation therapy. We plan to concurrently develop multiple product candidates targeting diseases with clear mechanisms of action and balancing research and development in IEM and oncology to maximize value.

Intellectual Property

Our success depends in part on our ability to obtain and maintain patents and other forms of intellectual property rights, including in-licenses of intellectual property rights of others, for our product candidates, methods used to manufacture our product candidates and methods for treating patients using our product candidates, as well as our ability to preserve our trade secrets, to prevent third parties from infringing upon our proprietary rights and to operate without infringing upon the proprietary rights of others. As of February 29, 2016, we are the owner of five U.S.

Patents, expiring between 2030 and 2031, absent any extensions, two of which are directed, respectively, to the compositions and methods of preparing AEB1102 (arginase), one directed to modified human arginase enzyme

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compositions, one directed to compositions of AEB2109 (methioninase) and their use in the treatment of cancer, and directed to recombinant nucleic acids encoding the methioninase enzyme employed to prepare AEB2109. As of February 29, 2016 we also owned three pending U.S. patent applications, two of which are related to pharmaceutical compositions of AEB1102, and one directed to methods for identifying and selecting primate cystathionine gamma-lyase variants having L-methionine degrading activity. As of February 29, 2016, we also controlled two US applications, exclusively licensed to us from the Board of Regents, The University of Texas System (Board), including one related to compositions of AEB2109 and one is related to compositions of AEB3103 (cysteine degrading enzyme) and their use in cancer treatment. Any patents issuing from the foregoing owned or licensed U.S. applications are expected to expire between 2029 and 2035, absent any adjustments or extensions. As of February 29, 2016, we owned a total of eight pending foreign applications and three patents in jurisdictions variously including: Australia, Canada, China, Europe, Japan, Hong Kong and South Korea. Any issued patents, or those issuing from these foreign patent applications, are expected to expire between 2029 and 2031, absent any adjustments or extensions. These foreign patent applications and patents variously comprise claims that relate to the compositions of AEB1102 and AEB2109 and methods of use of AEB1102 for the treatment of cancer. As of February 29, 2016, we also controlled fourteen pending international applications variously in Australia, Canada, China, EPO, Israel, Japan and Korea, also exclusively licensed to us from the Board, with claims directed to compositions and methods of use of AEB2109 and to AEB3103 compositions and methods of use. Any patents issuing from these applications are expected to expire in 2034, absent any adjustments or extensions.

Patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in various countries where patent protection is obtained. The actual protection afforded by a patent, which can vary from country to country, depends on the type of patent, the scope of its coverage and the availability of legal remedies in the country.

We also use other forms of protection, such as trademark, copyright and trade secret protection, to protect our intellectual property, particularly where we do not believe patent protection is appropriate or obtainable. We aim to take advantage of all of the intellectual property rights that are available to us and believe that this comprehensive approach will provide us with proprietary positions for our product candidates, where available.

We also protect our proprietary information by requiring our employees, consultants, contractors and other advisors to execute nondisclosure and assignment of invention agreements upon commencement of their respective employment or engagement. In addition, we also require confidentiality or service agreements from third parties that receive our confidential information or materials.

Licensing

On December 24, 2013, two of our wholly-owned subsidiaries, AECASE, Inc. (AECASE) and AEMASE, Inc. (AEMASE) entered into license agreements with the University of Texas at Austin (UTA) under which UTA has granted to AECASE and AEMASE exclusive, worldwide, sublicenseable licenses. UTA granted the AECASE license under a patent application relating to the right to use technology related to our AEB3103 product candidate. UTA granted the AEMASE license under a patent relating to the right to use technology related to our AEB2109 product candidate.

The licenses have identical terms. With respect to each product candidate covered by a license with UTA, AECASE or AEMASE could be required to pay UTA up to \$6.4 million milestone payments based on the achievement of certain development milestones, including clinical trials and regulatory approvals, the majority of which are due upon the achievement of later development milestones,

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including a \$5.0 million payment due on regulatory approval of a product and a \$500,000 payment payable on final regulatory approval of a product for a second indication. AECASE and AEMASE are also required to pay an annual license fee, ranging from \$5,000 to \$25,000. In addition, AECASE and AEMASE will pay UTA a low single digit royalty on worldwide-net sales of products covered under each license agreement, together with a revenue share on non-royalty consideration received from sublicensees. The rate of the revenue share depends on the date the sublicense agreement is signed. The rate is 30% for agreements signed in 2014, 25% for agreements signed in 2015, 20% for agreements signed in 2016, 15% for agreements signed in 2017 and 6.5% for agreements signed in 2018 and thereafter. The term of the license agreements continues until the expiration of the last to expire of the patents licensed thereunder. UTA may terminate the agreement for breach by AECASE or AEMASE that is not cured within 30 or 60 days of notice (depending on the type of breach) and three or more financial breaches in any nine month period which, even if cured, were not cured within 30 days of notice, or if AECASE or AEMASE or any of their respective affiliates or sublicensees participates in any proceeding to challenge the licensed patent rights (unless, with respect to sublicensees, AECASE or AEMASE terminates the applicable sublicense). As of December 31, 2015, we have paid \$31,000 under these license agreements.

Sponsored Research Agreement

In connection with the above license agreements, we and each of our wholly-owned subsidiaries also entered into a Sponsored Research Agreement, or SRA, with UTA on December 24, 2013, and amended on September 24, 2014, January 15, 2015, August 10, 2015, November 5, 2015 and January 7, 2016 wherein we agreed to sponsor research to be conducted at the laboratory of Professor George Georgiou at UTA related to the systemic depletion of amino acids for cancer therapy, and enzyme replacement for the treatment of patients having inborn metabolic defects. The SRA will expire on August 31, 2016, and we have the option of extending the research program under mutually agreeable support terms. We can terminate the SRA with 60 days' notice to UTA. UTA can terminate the SRA for our material breach that remains uncured 60 days after notice from UTA. With respect to intellectual property that results from the sponsored research, each party owns any such intellectual property that it solely creates and we jointly own with UTA any such intellectual property that we jointly create. We have an option to negotiate a license to UTA's interest in any such intellectual property and any such license agreement is expected to be on terms substantially similar to the existing license agreements described above. If we fail to enter into such a license agreement within six months of the date we exercise our option (or such longer period of time as we may mutually agree), UTA would be free to grant licenses in the applicable intellectual property to third parties. The maximum permitted cost of the sponsored research to us is approximately \$1.4 million. This increases if we agree to extend the research program beyond August 31, 2016. As of December 31, 2015, we have paid \$949,000 to UTA under the SRA.

Grant Agreement

In June 2015, we entered into a Cancer Research Grant Contract, or the Grant Contract, with the Cancer Prevention and Research Institute of Texas, or CPRIT, under which CPRIT awarded us a grant not to exceed \$19.8 million to be used to develop novel cancer treatments by exploiting the unique metabolism of cancer cells. As of December 31, 2015, we have recognized \$6.1 million in revenue under the Grant Contract. The Grant Contract will expire on May 31, 2017.

Pursuant to the Grant Contract, we grant to CPRIT a non-exclusive, irrevocable, royalty-free, perpetual, worldwide license to any technology and intellectual property resulting from the grant-funded activities and any other intellectual property that is owned by us and necessary for the exploitation of the technology and intellectual property resulting from the grant-funded activities (the "Project Results") for and on behalf of CPRIT and other governmental entities and agencies of the State of Texas and private or independent institutions of higher education located in Texas for education, research and

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other non-commercial purposes only. The terms of the Grant Contract require that we pay tiered royalties in the low-to mid-single digit percentages on revenues from sales and licenses of products or services that are based upon, utilize, are developed from or materially incorporate Project Results. Such royalties reduce to less than one percent after a mid-single-digit multiple of the grant funds have been repaid to CPRIT in royalties. Such royalties are payable for so long as we have marketing exclusivity or patents covering the applicable product or service (or twelve years from first commercial sale of such product or service in certain countries if there is no such exclusivity or patent protection).

If we abandon patent applications or patents covering Project Results in certain major market countries, CPRIT can, at its own cost, take over the prosecution and maintenance of such patents and is granted a non-exclusive, irrevocable, royalty-free, perpetual license with right to sublicense in such country to the applicable Project Results. We are required to use diligent and commercially reasonable efforts to commercialize at least one commercial product or service or otherwise bring to practical application the Project Results. If CPRIT notifies us of our failure with respect to the foregoing, and such failure is not owing to material safety concerns, then, at CPRIT's option, the applicable Project Results would be transferred to CPRIT and CPRIT would be granted a non-exclusive license to any other intellectual property that is owned by us and necessary for the exploitation of the Project Results, and CPRIT, at its own cost, can commercialize products or services that are based upon, utilize, are developed from or materially incorporate Project Results. CPRIT's option is subject to our ability to cure any failures identified by CPRIT within 60 days and a requirement to negotiate in good faith with us with respect to an alternative commercialization strategy for a period of 180 days.

Competition

While we believe that our nonclinical development experience and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, and ultimately biosimilar and generic drug companies. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

The acquisition or licensing of pharmaceutical products is also very competitive, and a number of more established companies, which have acknowledged strategies to license or acquire products, may have competitive advantages as may other emerging companies taking similar or different approaches to product acquisitions. These established companies may have a competitive advantage over us due to their size, cash flows, and institutional experience.

We compete in the segments of the pharmaceutical, biotechnology and other related markets that address IEM and cancer metabolism.

Inborn errors of metabolism. With respect to AEB1102 for Arginase I deficiency, there are currently no approved therapeutics that address the underlying cause of the disease and we are not aware of any other therapeutics that do so in clinical development. It is possible that competitors may produce, develop, and commercialize therapeutics, or utilize other approaches to treat Arginase I deficiency. The current method for treating patients with Arginase I deficiency is dietary restriction, which appears to slow the disease progression, as well as treatments such as Hyperion Therapeutics' RAVICTI (glycerol phenylbutyrate) and BUPHENYL (sodium benzoate) which lower blood-ammonia levels.

Cancer metabolism. With respect to our oncology product candidates, we compete with other companies that pursue a cancer metabolism approach, as well as companies that employ more common methods of treating patients such as surgery, radiation and drug therapy. These drug

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therapies include chemotherapy, hormone therapy and targeted drug, including biological product, therapy.

There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While our product candidates may compete with many existing drug and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our product candidates will not be competitive with them. Some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well-established therapies and are widely accepted by physicians, patients and third-party payors. In general, although there has been considerable progress over the past few decades in the treatment of cancer and the currently marketed therapies provide benefits to many patients, these therapies all are limited to some extent in their efficacy and frequency of adverse events, and none are successful in treating all patients. As a result, the level of morbidity and mortality from cancer remains high.

In addition to currently marketed therapies, there are also a number of medicines in late-stage clinical development to treat cancer. While there are currently no approved drugs targeting tumor arginine dependence, we are aware of a number of compounds that are in clinical development and enrolling patients with solid and hematological malignancies, including Polaris Group's microbial ADI-PEG 20 and Biocancer Treatment International's pegylated native human Arginase I. Additionally, Calithera Biosciences is targeting a therapy that inhibits Arginase I as an immune modulator. These medicines in development may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies. As a result, they may provide significant competition for our product candidate AEB1102.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, nonclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved medicines than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. 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 all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of assays or tests that are essential to identifying an appropriate patient population, which we refer to as companion diagnostics, in guiding the use of related therapeutics, the level of biosimilar competition and the availability of reimbursement from government and other third-party payors.

Manufacturing

We currently contract with third parties for the manufacturing and testing of our product candidates for nonclinical studies and intend to do so for our future clinical studies as well. We intend to identify and qualify additional manufacturers to provide potential alternative sources for the active pharmaceutical ingredient and fill-and-finish services for AEB1102 as the compound progresses through clinical development, prior to seeking marketing approval from FDA. We believe we have sufficient supplies of AEB1102 for our planned Phase 1 and Phase 2 trials.

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The KBI Agreement

In December 2013, we entered into a Master Services Agreement, or KBI Agreement, with KBI Biopharma, Inc., or KBI, in which KBI agreed to research, develop and manufacture the active pharmaceutical ingredient for AEB1102 in exchange for cash and shares of our Series A convertible preferred stock. In June 2015, we amended the KBI Agreement to also permit us to exchange Series B convertible preferred stock for such research, development and manufacturing services. The KBI Agreement was further amended in June 2015 to convert the remaining unmet milestone awards from share-based payments to cash. The KBI Agreement has an initial three-year term and automatically renews for successive additional one-year terms until the services are completed. The KBI Agreement may be terminated by either party for a breach that is not remedied within thirty days after notice or in the event of a bankruptcy by either party. We may terminate the KBI Agreement upon sixty-days written notice. For termination other than a material breach by KBI, we must pay for all services conducted prior to the termination and to wind down the activities.

The LSNE Agreement

In November 2014, we entered into a Master Services Agreement, or LSNE Agreement, with Lyophilization Services of New England, Inc., or LSNE, in which LSNE agreed to manufacture the finished product of AEB1102 for clinical testing in exchange for cash. The LSNE Agreement has a one-year term that we may unilaterally extend for successive one-year periods upon written notice. The LSNE Agreement may be terminated for either party for a material breach that is not remedied within thirty-days after notice or in the event of a bankruptcy by either party. We may terminate the contract for convenience upon written notice, but must pay termination fees.

We do not own or operate manufacturing facilities for the production of clinical quantities of our product candidates. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. The use of contracted manufacturing is relatively cost-efficient and has eliminated the need for our direct investment in manufacturing facilities and additional staff early in development.

For our biomarker and companion diagnostic strategies, we will rely on third-party vendors for the development and execution of our tests. If we choose to develop a biomarker-based test including a companion diagnostic for any of our therapeutic enzymes, we may rely on one or more third parties to manufacture and sell a single test.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

FDA approval process

In the United States, pharmaceutical products are subject to extensive regulation by the United States Food and Drug Administration, or the FDA. The Federal Food, Drug, and Cosmetic Act, or the FDC Act, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting,

sampling, and import and export of pharmaceutical products. Biological products used for the prevention, treatment, or cure of a disease

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or condition of a human being are subject to regulation under the FDC Act, except the section of the FDC Act which governs the approval of new drug applications, or NDAs. Biological products are approved for marketing under provisions of the Public Health Service Act, or PHSA, via a Biologics License Application, or BLA. However, the application process and requirements for approval of BLAs are very similar to those for NDAs, and biologics are associated with similar approval risks and costs as drugs. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as clinical hold, FDA refusal to approve pending NDAs or BLAs, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, and criminal prosecution.

Biological product development for a new product or certain changes to an approved product in the United States typically involves preclinical laboratory and animal tests, the submission to the FDA of an investigational new drug application, or IND, which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity, and novelty of the product or disease.

Preclinical tests include laboratory evaluation of product chemistry, formulation, and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements, including good laboratory practices. The results of preclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted. A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin. Clinical trials involve the administration of the investigational biologic to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with good clinical practice, or GCP, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators, and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The trial protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board, or IRB, for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Clinical trials to support BLAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the biologic into healthy human subjects or patients, the product is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence on effectiveness. Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the drug or biologic for a particular indication, dosage tolerance, and optimal dosage, and to identify common adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to

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obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit the FDA to evaluate the overall benefit-risk relationship of the drug or biologic and to provide adequate information for the labeling of the product. In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the biologic. A single Phase 3 trial with other confirmatory evidence may be sufficient in rare instances where the trial is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible.

After completion of the required clinical testing, a BLA is prepared and submitted to the FDA. FDA approval of the BLA is required before marketing of the product may begin in the United States. The BLA must include the results of all preclinical, clinical, and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture, and controls. The cost of preparing and submitting a BLA is substantial. The submission of most BLAs is additionally subject to a substantial application user fee, currently exceeding \$2,374,000 for U.S. Government Fiscal Year 2016, and the applicant under an approved BLA is also subject to annual product and establishment user fees, currently exceeding \$114,000 per product and \$585,000 per establishment for U.S. Government Fiscal Year 2016. These fees are typically increased annually. The FDA has 60 days from its receipt of a BLA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of BLAs. Most such applications for standard review biologic products are reviewed within ten months of the date the FDA files the BLA; most applications for priority review biologics are reviewed within six months of the date the FDA files the BLA. Priority review can be applied to a biologic that the FDA determines has the potential to treat a serious or life-threatening condition and, if approved, would be a significant improvement in safety or effectiveness compared to available therapies. The review process for both standard and priority review may be extended by the FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission.

The FDA may also refer applications for novel biologic products, or biologic products that present difficult questions of safety or efficacy, to an advisory committee—typically a panel that includes clinicians and other experts—for review, evaluation, and a 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 a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the biologic product is manufactured. The FDA will not approve the product unless compliance with current good manufacturing practice, or cGMP, is satisfactory and the BLA contains data that provide substantial evidence that the biologic is safe, pure, potent and effective in the indication studied.

After the FDA evaluates the BLA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or information, in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the BLA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. An approval letter authorizes commercial marketing of the biologic with specific prescribing information for specific indications. As a condition of BLA approval, the FDA may require a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the biologic outweigh the potential risks. REMS can include medication guides, communication plans for healthcare

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professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the product. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the product's safety or efficacy.

Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing. Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new BLA or BLA supplement before the change can be implemented. A BLA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing BLA supplements as it does in reviewing BLAs.

Fast track designation and accelerated approval

The FDA is required to facilitate the development, and expedite the review, of biologics that are intended for the treatment of a serious or life-threatening disease or condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the condition. Under the fast track program, the sponsor of a new biologic candidate may request that the FDA designate the candidate for a specific indication as a fast track biologic concurrent with, or after, the filing of the IND for the candidate. The FDA must determine if the biologic candidate qualifies for fast track designation within 60 days of receipt of the sponsor's request. Under the fast track program and FDA's accelerated approval regulations, the FDA may approve a biologic for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments.

In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions, or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A biologic candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval trials, or confirm a clinical benefit during post-marketing trials, will allow the FDA to withdraw the biologic from the market on an expedited basis. All promotional materials for biologic candidates approved under accelerated regulations are subject to prior review by the FDA.

In addition to other benefits such as the ability to use surrogate endpoints and engage in more frequent interactions with the FDA, the FDA may initiate review of sections of a fast track product's BLA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing an application does not begin until the last section of the BLA is submitted. Additionally, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Breakthrough therapy designation

The FDA is also required to expedite the development and review of the application for approval of biological products that are intended to treat a serious or life-threatening disease or condition where

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preliminary clinical evidence indicates that the biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. Under the breakthrough therapy program, the sponsor of a new biologic candidate may request that the FDA designate the candidate for a specific indication as a breakthrough therapy concurrent with, or after, the filing of the IND for the biologic candidate. The FDA must determine if the biological product qualifies for breakthrough therapy designation within 60 days of receipt of the sponsor's request.

Orphan drug designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to biological products intended to treat a rare disease or condition—generally a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a product available in the United States for such disease or condition will be recovered from sales of the product.

Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the generic identity of the biological product and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first BLA applicant to receive FDA approval for a particular active moiety to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that product for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market a biological product containing the same active moiety for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. A product is clinically superior if it is safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biological product for the same disease or condition, or the same biological product for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA user fee.

Disclosure of clinical trial information

Sponsors of clinical trials of FDA-regulated products, including biological products, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, trial sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Pediatric information

Under the Pediatric Research Equity Act, or PREA, NDAs or BLAs or supplements to NDAs or BLAs must contain data to assess the safety and effectiveness of the biological product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the biological product is safe and effective. The FDA may grant full or partial waivers, or deferrals, for submission of data. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted.

Additional controls for biologics

To help reduce the increased risk of the introduction of adventitious agents, the PHSA emphasizes the importance of manufacturing controls for products whose attributes cannot be precisely defined. The PHSA also provides authority to the FDA to immediately suspend licenses in situations where there exists a danger to public health, to prepare or procure products in the event of shortages and critical public health needs, and to authorize the creation and enforcement of regulations to prevent the introduction or spread of communicable diseases in the United States and between states.

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After a BLA is approved, the product may also be subject to official lot release as a condition of approval. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA may also perform certain confirmatory tests on lots of some products, such as viral vaccines, before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products. As with drugs, after approval of biologics, manufacturers must address any safety issues that arise, are subject to recalls or a halt in manufacturing, and are subject to periodic inspection after approval.

Patent term restoration

After approval, owners of relevant drug or biologic patents may apply for up to a five year patent extension. The allowable patent term extension is calculated as half of the drug's testing phase—the time between IND application and NDA or BLA submission—and all of the review phase—the time between NDA or BLA submission and approval up to a maximum of five years. The time can be shortened if FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years.

For patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the United States Patent and Trademark Office must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for a drug or biologic for which an NDA or BLA has not been submitted.

Biosimilars

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, creates an abbreviated approval pathway for biological products shown to be highly similar to or interchangeable with an FDA-licensed reference biological product. Biosimilarity sufficient to reference a prior FDA-approved product requires that there be no differences in conditions of use, route of administration, dosage form, and strength, and no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency. Biosimilarity must be shown through analytical trials, animal trials, and a clinical trial or trials, unless the Secretary of Health and Human Services waives a required element. A biosimilar product may be deemed interchangeable with a prior approved product if it meets the higher hurdle of demonstrating that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. On March 6, 2015, the FDA approved the first biosimilar product under the BPCIA. Complexities associated with the larger, and often more complex, structures of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation, which is still being evaluated by the FDA.

A reference biologic is granted 12 years of exclusivity from the time of first licensure of the reference product, and no application for a biosimilar can be submitted for four years from the date of licensure of the reference product. The first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against a finding of interchangeability for other biologics for the same condition of use for the lesser of (i) one year after first commercial marketing of the first interchangeable biosimilar, (ii) 18

months after the first

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interchangeable biosimilar is approved if there is no patent challenge, (iii) eighteen months after resolution of a lawsuit over the patents of the reference biologic in favor of the first interchangeable biosimilar applicant, or (iv) 42 months after the first interchangeable biosimilar's application has been approved if a patent lawsuit is ongoing within the 42-month period.

Post-approval requirements

Once a BLA is approved, a product will be subject to certain post-approval requirements. For instance, the FDA closely regulates the post-approval marketing and promotion of biologics, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. Biologics may be marketed only for the approved indications and in accordance with the provisions of the approved labeling.

Adverse event reporting and submission of periodic reports is required following FDA approval of a BLA. The FDA also may require post-marketing testing, known as Phase 4 testing, REMS, and surveillance to monitor the effects of an approved product, or the FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control, biological product manufacture, packaging, and labeling procedures must continue to conform to cGMPs after approval. Biologic manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced inspections by the FDA, during which the agency inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money, and effort in the areas of production and quality-control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

FDA regulation of companion diagnostics

If use of an *in vitro* diagnostic is essential to safe and effective use of a drug or biologic product, then the FDA generally will require approval or clearance of the diagnostic, known as a companion diagnostic, at the same time that the FDA approves the therapeutic product. The FDA has generally required *in vitro* companion diagnostics intended to select the patients who will respond to cancer treatment to obtain a pre-market approval, or PMA, for that diagnostic simultaneously with approval of the therapeutic. The review of these *in vitro* companion diagnostics in conjunction with the review of a cancer therapeutic involves coordination of review by the FDA's Center for Biologics Evaluation and Research and by the FDA's Center for Devices and Radiological Health.

The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee, which exceeds \$250,000 for most PMAs. In addition, PMAs for certain devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, the applicant must demonstrate that the diagnostic produces reproducible results when the same sample is tested multiple times by multiple users at multiple laboratories. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation, or QSR, which imposes elaborate testing, control, documentation and other quality assurance requirements.

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PMA approval is not guaranteed, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay approval. If the FDA's evaluation of the PMA application is favorable, the FDA typically issues an approvable letter requiring the applicant's agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the United States.

Other U.S. healthcare laws and compliance requirements

In the United States, our activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including but not limited to, the Centers for Medicare and Medicaid Services, or 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, or DOJ, and individual U.S. Attorney offices within the DOJ, and state and local governments. For example, sales, marketing and scientific/educational grant programs must comply with the anti-fraud and abuse provisions of the Social Security Act, the false claims laws, the privacy provisions of the Health Insurance Portability and Accountability Act, or HIPAA, and similar state laws, each as amended.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor.

Additionally, the intent standard under the Anti-Kickback Statute was amended by the Affordable Care Act, or ACA, to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In

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addition, the ACA codified case law 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 federal False Claims Act (discussed below).

The civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The federal False Claims Act prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes any request or demand for money or property presented to the U.S. government. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus generally non-reimbursable, uses.

HIPAA created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. We may be subject to data privacy and security regulations by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, imposes requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates, independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Additionally, the federal Physician Payments Sunshine Act within the ACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members.

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In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of drug and biological products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical and biotechnology companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical and biotechnology companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private *qui tam* actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Coverage, pricing and reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage, and establish adequate reimbursement levels for such products. In the United States, third-party payors include federal and state healthcare programs, private managed care providers, health insurers and other organizations. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price of a product or for establishing the reimbursement rate that such a payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication. Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. We may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Our product candidates may not be considered medically necessary or cost-effective. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. 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.

Different pricing and reimbursement schemes exist in other countries. In the EU, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may

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only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any product candidates for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on healthcare pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare reform

In March 2010, President Obama enacted the ACA, which has the potential to substantially change healthcare financing and delivery by both governmental and private insurers, and significantly impact the pharmaceutical and biotechnology industry. The ACA will impact existing government healthcare programs and will result in the development of new programs.

Among the ACA provisions of importance to the pharmaceutical and biotechnology industries, in addition to those otherwise described above, are the following:

- n an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs, that began in 2011;
- n an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, retroactive to January 1, 2010, to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price, or AMP;
- n 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 manufacturers' outpatient drugs to be covered under Medicare Part D;
- n extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- n expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals beginning in 2014 and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- n expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; and
- n a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

We anticipate that the ACA will result in additional downward pressure on coverage and the price that we receive for any approved product, and could seriously harm our business. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare

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reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. In addition, it is possible that there will be further legislation or regulation that could harm our business, financial condition and results of operations.

The Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Additional regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

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 of 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 much like the IND prior to the commencement of human clinical trials. In the EU, for example, a clinical trial application must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the clinical trial application is approved in accordance with a country's requirements, clinical trial development may proceed. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

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 GCP 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 or biological product under EU regulatory systems, we must submit a marketing authorization application. The application used to file the BLA in the United States is similar to that required in the EU, with the exception of, among other things, country-specific document requirements.

For other countries outside of the EU, 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 are conducted in accordance with

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GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we or our potential collaborators 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.

Legal Proceedings

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity and reputational harm, and other factors.

Facilities

Our corporate headquarters are located in Austin, Texas where we occupy approximately 5,800 square feet of office space under a lease which expires in 2017. We use these facilities for administration, research and product development activities. We do not have our own research laboratories.

We intend to procure additional office and laboratory space as we add employees and expand geographically. We believe that our facilities are adequate to meet our needs for the immediate future, and that, should it be needed, suitable additional space will be available to accommodate any such expansion of our operations.

Employees

As of February 29, 2016, we had a total of 23 full-time employees, all located in the United States. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We have not experienced any work stoppages, and we consider our relations with our employees to be good.

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The following table provides information regarding our executive officers and directors as of March 25, 2016:

Name	Age	Position
Executive Officers:		
David G. Lowe, Ph.D.	59	Chief Executive Officer, President and Director
Henry L. Hebel	44	Vice President, Product Development
Scott W. Rowlinson, Ph.D.	48	Vice President, Research
Joseph E. Tyler	65	Vice President, Manufacturing
Charles N. York II	39	Chief Financial Officer and Vice President
Non-Employee Directors:		
Armen Shanafelt, Ph.D.(1)(2)	56	Director
Henry Skinner, Ph.D.*	52	Director
George Georgiou, Ph.D.	56	Director
Sandesh Mahatme(1)(2)(3)	51	Director
Russell J. Cox(1)(2)(3)	52	Director
Anthony G. Quinn, M.B Ch.B, Ph.D.	54	Director

(1) Member of our audit committee.

(2) Member of our compensation committee.

(3) Member of our nominating and corporate governance committee.

* Dr. Skinner resigned from our board of directors effective immediately prior to the effectiveness of the registration statement of which this prospectus forms a part.

Executive Officers

David G. Lowe, Ph.D. Dr. Lowe is our co-founder and has served as our Chief Executive Officer and President and as a member of our board of directors since December 2013. From June 2002 to November 2012, Dr. Lowe served at Skyline Ventures, a venture capital firm initially as a Kauffman Fellow from June 2002 to December 2003 then as a Partner and Managing Director. From 1985 to 2001, Dr. Lowe served in positions of increasing responsibility at Genentech Inc., initially as a post doctoral fellow and ultimately as a Research Director. Dr. Lowe holds a B.Sc. and Ph.D. in Biochemistry from the University of Toronto. We believe that Dr. Lowe should serve as a member of our board of directors due to the perspective he brings as our founder and his expertise in the fields of business and therapeutics.

Henry L. Hebel. Mr. Hebel joined our company in May 2015 as Vice President, Operations and was appointed Vice President, Product Development in October 2015. Since June 2014, Mr. Hebel has served as the President of The Hebel Consulting Group. From February 2012 to June 2014, Mr. Hebel served as the Vice President of Drug Development for Terapio Corp. Additionally, Mr. Hebel was Chief Operating Officer of VGXI Inc. from April 2001 to January 2012. Prior to VGXI, Mr. Hebel served in various product development management and operations roles at Qiagen, Inc., Gene Medicine Inc., and Tanox Biosystems, Inc. Mr. Hebel holds a B.S. in Zoology and an MBA from Texas A&M University.

Scott W. Rowlinson, Ph.D. Dr. Rowlinson, joined our company as Vice President, Research in February 2014. From May 2000 to February 2014, Dr. Rowlinson worked as a research scientist at Eli

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Lilly & Company, a pharmaceutical company. Dr. Rowlinson holds a B.S. in Physiology & Pharmacology and a Ph.D. in Physiology and Pharmacology from the University of Queensland, Australia.

Joseph E. Tyler. Mr. Tyler joined our company as Vice President, Manufacturing in December 2013. Since November 2006, Mr. Tyler has also provided consulting services to Pharm Supply Inc., a chemistry manufacturing and controls company, and Proteon Therapeutics, Inc., a pharmaceuticals development company. Mr. Tyler previously worked as Vice President, Manufacturing of KBI Biopharma Inc., a biopharmaceutical development and manufacturing company from January until November 2011 and Program Head of Vance Granville Community College from August 2008 to January 2011. Mr. Tyler received a B.S. in Chemical Engineering from Carnegie Mellon University and an M.S. in Biochemical Engineering from Cornell University.

Charles N. York II. Mr. York joined our company as Vice President, Finance, in July 2014 and was appointed Chief Financial Officer and Vice President, in September 2015. Prior to joining our company, Mr. York served as CFO Consultant of Bridgepoint Consulting, a finance consulting company, where he focused on life science, pharmaceutical and healthcare companies, from March 2013 to June 2014. From March 2009 to August 2012, Mr. York was the corporate controller of Astrotech Corporation, an aerospace company. Prior to that, Mr. York held financial management roles at Arthrocare Corp. and Freescale Semiconductor Inc. Mr. York began his career at PricewaterhouseCoopers LLP. Mr. York is a CPA in the state of Arizona and received a B.S. in Accounting from the University of Connecticut and an MBA from the University of Texas at Austin.

Non-Employee Directors

Armen Shanafelt, Ph.D. Dr. Shanafelt has served as a director since December 2013 and has served as Chairman of our board of directors since February 2014. Since April 2009, Dr. Shanafelt has been a partner of Lilly Ventures, a venture capital firm. Previous to joining Lilly Ventures, Dr. Shanafelt was Chief Science Officer responsible for the generation of the early biotherapeutic pipeline for Eli Lilly and Company, a pharmaceutical research company, spanning the therapeutic areas of oncology, endocrine, and neuroscience. Dr. Shanafelt received his B.S. in Chemistry and Physics from Pacific Lutheran University, and his Ph.D. in Chemistry from the University of California, Berkeley. He completed his postdoctoral work at DNAX Research Institute, where he studied the structure-function relationships of cytokines and their receptors. We believe Dr. Shanafelt is qualified to serve on our board of directors because of his experience in the pharmaceutical, biotechnology and diagnostic businesses, including his expertise with respect to the generation of early biotherapeutic pipelines for oncology therapeutics.

Henry Skinner, Ph.D. Dr. Skinner has served as a director since December 2013. Since November 2008, Dr. Skinner has been a managing director of Novartis Venture Funds. Dr. Skinner earned his Ph.D. in Microbiology and M.S. in Biochemistry from the University of Illinois. He was a postdoctoral fellow at Baylor College of Medicine in the department of Human and Molecular Genetics and received his B.S. in biology and biotechnology from Worcester Polytechnic Institute. We believe Dr. Skinner is qualified to serve on our board of directors because of his expertise with respect to therapeutic technologies.

George Georgiou, Ph.D. Dr. Georgiou has served as a director since December 2013. Since August 1986, Dr. Georgiou has served on the faculties of Chemical Engineering, Biomedical Engineering and Molecular Biosciences at the University of Texas at Austin. Since September 2014, Dr. Georgiou has served as manager of Kyn Therapeutics LLC and, since January 2012, as manager of GMA L.L.C. He received his B.Sc. in Chemical Engineering from the University of Manchester, U.K. and his Ph.D. from Cornell University. Dr. Georgiou was elected member of the National Academy of Engineering (NAE) in 2005 and to the U.S. Institute of Medicine (IOM) of the National Academy of

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Sciences in 2011. We believe Dr. Georgiou is qualified to serve on our board of directors because of his experience developing protein therapeutics and analyzing adaptive immune responses.

Sandesh Mahatme. Mr. Mahatme has served as a director since June 2015. Since November 2012, Mr. Mahatme has served as Senior Vice President and Chief Financial Officer at Sarepta Therapeutics, Inc., a publicly traded biopharmaceutical company. From January 2006 to November 2012, Mr. Mahatme worked at Celgene Corporation, a publicly traded biopharmaceutical company, where he served in various roles, including Senior Vice President of Corporate Development, Senior Vice President of Finance, Corporate Treasurer and Head of Tax. From 1997 to 2005 Mr. Mahatme worked for Pfizer Inc., a pharmaceutical company, where he served in senior roles in business development and corporate tax. Mr. Mahatme earned LL.M. degrees from Cornell Law School and NYU School of Law and is a member of the New York State Bar Association. He is a director at Flexion Therapeutics, Inc., a publicly traded specialty pharmaceutical company. We believe Mr. Mahatme is qualified to serve on our board of directors because of his experience in the pharmaceutical industry and financial expertise.

Russell J. Cox. Mr. Cox has served as a director since June 2015. Mr. Cox has served as Executive Vice President and Chief Operating Officer at Jazz Pharmaceuticals plc, a publicly traded biopharmaceutical company, since May 2014, where he also served as Executive Vice President and Chief Commercial officer from March 2012 to May 2014 and as Senior Vice President, Sales and Marketing from July 2010 until February 2012. Prior to that, he served in a variety of senior management roles since joining Jazz Pharmaceuticals, Inc. (the predecessor to Jazz Pharmaceutical plc) in July 2010. From January 2009 to January 2010, he was Senior Vice President and Chief Commercial Officer of Ipsen Group, a publicly traded pharmaceutical company, and from 2007 until December 2008, he was Vice President of Marketing at Tercica, Inc. (acquired by Ipsen Group), a biotechnology company. From 2003 to 2007, he was with Scios Inc. (acquired by Johnson and Johnson in 2003), where he also held the role of Vice President, Marketing. Prior to 2003, Mr. Cox was with Genentech, Inc. for 12 years, where he was a Product Team Leader responsible for the Growth Hormone franchise and led numerous product launches as a Group Product Manager. Mr. Cox received a B.S. in Biomedical Science from Texas A&M University. We believe Mr. Cox is qualified to serve on our board of directors due to his experience in the biopharmaceutical industry.

Anthony G. Quinn, M.B Ch.B, Ph.D. Dr. Quinn has served as a director since March 2016. Since October 2015, Dr. Quinn has worked as a private consultant for IDBioPharm Consulting LLC. From August 2009 to June 2015, Dr. Quinn served as Head of Research & Development and Chief Medical Officer initially at the Senior Vice President level and subsequently at the Executive Vice President level for Synageva BioPharma Corp., a publicly traded biopharmaceutical company that was acquired by Alexion Pharmaceuticals, Inc. in June 2015. Following the acquisition, Dr. Quinn worked for Alexion Pharmaceuticals from June 2015 to September 2015. Dr. Quinn received a B.MSc in General Pathology and a M.B Ch.B in Medicine from the University of Dundee. Dr. Quinn later earned a Ph.D. in Cancer Research from the University of Newcastle upon Tyne. We believe Dr. Quinn is qualified to serve on our board of directors because of his experience in the biopharmaceutical industry.

Family Relationships

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

Board Composition

Our business and affairs are organized under the direction of our board of directors, which will consist of six members following this offering. The primary responsibilities of our board of directors are to provide oversight, strategic guidance, counseling and direction to our management. Our board of directors meets on a regular basis and additionally as required.

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Immediately following this offering, our board of directors will be divided into three staggered classes of directors. At each annual meeting of stockholders, a class of directors will be elected for a three-year term to succeed the same class whose term is then expiring. As a result, only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. Our directors will be divided among the three classes as follows:

- n the Class I directors will be Mr. Mahatme and Dr. Georgiou, and their terms will expire at the annual meeting of stockholders to be held in 2017; and
- n the Class II directors will be Mr. Cox and Dr. Lowe, and their terms will expire at the annual meeting of stockholders to be held in 2018; and
- n the Class III directors will be Dr. Shanafelt and Dr. Quinn, and their terms will expire at the annual meeting of stockholders to be held in 2019.

Each director's term continues until the election and qualification of his successor, or his earlier death, resignation or removal. Our restated certificate of incorporation and restated bylaws that will be in effect upon the completion of this offering authorize only our board of directors to fill vacancies on our board of directors. Any increase or decrease in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. This classification of our board of directors may have the effect of delaying or preventing changes in control of our company. See Description of Capital Stock Anti-Takeover Provisions Restated Certificate of Incorporation and Restated Bylaw Provisions.

Director Independence

In connection with this offering, our common stock will be listed on The NASDAQ Global Market. Under the rules of The NASDAQ Global Market, independent directors must comprise a majority of a listed company's board of directors within a specified period of the completion of this offering. In addition, the rules of The NASDAQ Global Market require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent. Under the rules of The NASDAQ Global Market, a director will only qualify as an independent director if, in the opinion of that 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.

Our board of directors has undertaken a review of the independence of each director and considered whether each director has a material relationship with us that could compromise his ability to exercise independent judgment in carrying out his responsibilities. As a result of this review, our board of directors determined that each of Mr. Cox, Dr. Quinn, Mr. Mahatme and Dr. Shanafelt are independent directors as defined under the applicable rules and regulations of the Securities and Exchange Commission, or SEC, and the listing requirements and rules of The NASDAQ Global Market. In making these determinations, our board of directors reviewed and discussed information provided by the directors and us with regard to each director's business and personal activities and relationships as they may relate to us and our management, including the beneficial ownership of our capital stock by each non-employee director and the transactions involving them described in the section titled Certain Relationships and Related Party Transactions.

Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended, or Exchange Act. 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: (1) accept, directly or indirectly, any consulting, advisory or other

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compensatory fee from the listed company or any of its subsidiaries; or (2) be an affiliated person of the listed company or any of its subsidiaries. We intend to satisfy the audit committee independence requirements of Rule 10A-3 upon the completion of this offering.

Committees of the Board of Directors

Our board of directors has an audit committee, a compensation committee and a nominating and corporate governance committee, each of which will have the composition and responsibilities described below upon completion of this offering. Upon completion of this offering, each of the below committees will have a written charter approved by our board of directors. Upon completion of this offering, copies of each charter will be posted on the Investor Relations section of our website. Members serve on these committees until their resignation or until otherwise determined by our board of directors.

Audit Committee

Our audit committee is composed of Mr. Mahatme, Mr. Cox and Dr. Shanafelt. Mr. Mahatme is the chairperson of our audit committee. Our board of directors has determined that Mr. Mahatme, Mr. Cox and Dr. Shanafelt are independent under the rules and regulations of the SEC and the listing standards of The NASDAQ Global Market applicable to audit committee members. Dr. Shanafelt is a General Partner of LV Management Group, LLC, the management company for Lilly Ventures Fund I, LLC, which we expect to beneficially own more than 10% of our common stock following this offering. Therefore, we may not be able to rely upon the safe harbor position of Rule 10A-3 under the Exchange Act, which provides that a person will not be deemed to be an affiliate of a company if he or she is not the beneficial owner, directly or indirectly, of more than 10% of a class of voting equity securities of that company. However, our board of directors has made an affirmative determination that Dr. Shanafelt is not an affiliate of our company. Each member of our audit committee is financially literate. In addition, our board of directors has determined that Mr. Mahatme is an audit committee financial expert as defined in Item 407(d)(5)(ii) of Regulation S-K promulgated under the Securities Act. This designation does not impose on him any duties, obligations or liabilities that are greater than those that are generally imposed on members of our audit committee and our board of directors. Our audit committee is directly responsible for, among other things:

- n selecting a firm to serve as the independent registered public accounting firm to audit our consolidated financial statements;
- n ensuring the independence of the independent registered public accounting firm;
- n discussing the scope and results of the audit with the independent registered public accounting firm, and reviewing, with management and that firm, our interim and year-end operating results;
- n establishing procedures for employees to anonymously submit concerns about questionable accounting or audit matters;
- n considering the adequacy of our internal controls and internal audit function;
- n reviewing material related party transactions or those that require disclosure; and
- n approving or, as permitted, pre-approving all audit and non-audit services to be performed by the independent registered public accounting firm.

Compensation Committee

Our compensation committee is composed of Mr. Mahatme, Mr. Cox and Dr. Shanafelt. Mr. Cox is the chairperson of our compensation committee. Each member of this committee is a non-employee director, as defined by Rule 16b-3 promulgated under the Exchange Act, and an outside director, as defined pursuant to Section 162(m) of the Internal

Revenue Code of 1984, as amended, or the Code, and each member of this committee meets the requirements for independence under the current

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NASDAQ Global Market listing standards and SEC rules and regulations. Our compensation committee is responsible for, among other things:

- n reviewing and approving, or recommending that our board of directors approve, the compensation of our executive officers;
- n reviewing and recommending to our board of directors the compensation of our directors;
- n reviewing and recommending to our board of directors the terms of any compensatory agreements with our executive officers;
- n administering our stock and equity incentive plans;
- n reviewing and approving, or making recommendations to our board of directors with respect to, incentive compensation and equity plans; and
- n reviewing our overall compensation philosophy.

Nominating and Governance Committee

Our nominating and governance committee is composed of Mr. Cox and Mr. Mahatme. Mr. Cox is the chairperson of our nominating and governance committee. Each member of this committee meets the requirements for independence under the current NASDAQ Global Market listing standards. Our nominating and governance committee is responsible for, among other things:

- n identifying and recommending candidates for membership on our board of directors;
- n recommending directors to serve on board committees;
- n reviewing and recommending our corporate governance guidelines and policies;
- n reviewing proposed waivers of the code of conduct for directors and executive officers;
- n evaluating, and overseeing the process of evaluating, the performance of our board of directors and individual directors; and
- n assisting our board of directors on corporate governance matters.

Compensation Committee Interlocks and Insider Participation

None of our executive officers has served as a member of the board of directors, or as a member of the compensation or similar committee, of any entity that has one or more executive officers who served on our board of directors or compensation committee during the year ended December 31, 2015. Prior to establishing the compensation committee, our full board of directors made decisions relating to the compensation of our officers. For a description of any transactions between us and members of our compensation committee and affiliates of such members, please see Certain Relationships and Related Party Transactions.

Codes of Business Conduct and Ethics

In connection with this offering, our board of directors has adopted a code of business conduct and ethics that applies to all of our employees, officers and directors, including our Chief Executive Officer and other executive officers. The full text of our codes of conduct will be posted on the Investor Relations section of our website. We intend to disclose future amendments to certain provisions of our codes of conduct, or waivers of these provisions, on our website or in public filings.

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The following tables and accompanying narrative disclosure set forth information about the compensation provided to our Chief Executive Officer and President, Dr. David G. Lowe; our Vice President, Product Development, Henry L. Hebel; and our Vice President, Research, Dr. Scott W. Rowlinson during the year ended December 31, 2015.

We refer to Dr. Lowe, Mr. Hebel and Dr. Rowlinson in this section as our Named Executive Officers.

Summary Compensation Table

The following table presents summary information regarding the total compensation for services rendered in all capacities that was awarded to, earned by and paid to our Named Executive Officers during the years ended December 31, 2014 and December 31, 2015.

Name and Principal Position	Fiscal Year	Salary (\$)	Bonus (\$)(1)	Equity Awards (\$)(2)	All Other Compensation (\$)	Total (\$)
<i>David G. Lowe, Ph.D.</i>	2015	382,500	66,900	522,016	14,255(3)	985,671
<i>Chief Executive Officer</i>	2014	375,000	111,563	295,964	15,614(3)	798,141
<i>Henry L. Hebel</i>	2015	144,000	28,800	207,281	78,961(4)	459,042
<i>Vice President, Product Development</i>						
<i>Scott W. Rowlinson, Ph.D.</i>	2015	249,538	49,800	118,789	14,851(3)	432,978
<i>Vice President, Research</i>	2014	203,968	40,794	34,312	15,518(3)	294,592

- (1) Discretionary cash bonuses earned in 2015 and paid in 2016, based in part on achievement of specified milestones and performance objectives. Amounts for 2014 represent discretionary cash bonuses earned in 2014, and paid in 2015, based in part on achievement of specified milestones and performance objectives.
- (2) The amounts reported in this column represent the aggregate grant date fair value of the awards granted to our Named Executive Officers during the years ended December 31, 2014 and 2015, as computed in accordance with Accounting Standards Codification Topic 718. The assumptions used in calculating the grant date fair value of the awards reported in the Equity Awards column are set forth in Note 9 to our consolidated financial statements. Note that the amounts reported in this column reflect the aggregate accounting cost for these awards, and do not necessarily correspond to the actual economic value that may be received by the Named Executive Officers from the awards.
- (3) Represents a health insurance premium paid by us in the applicable period on behalf of each of our Named Executive Officers.
- (4) Represents (i) pre-employment consulting fees of \$71,369 and (ii) a health insurance premium paid by us in the applicable period for on behalf of Mr. Hebel of \$7,592.

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Employment Agreements

David G. Lowe, Ph.D.

Pursuant to an executive employment agreement dated July 7, 2015 that was approved by our board of directors, or the Employment Agreement, Dr. Lowe serves as our Chief Executive Officer. Dr. Lowe's Employment Agreement sets forth the principal terms and conditions of his employment, including his initial annual base salary of \$382,500, an annual target cash bonus opportunity of 35% of his base salary (which bonus is earned based on our achievement of specified milestones and performance objectives, as well as Dr. Lowe's performance relative to one or more performance objectives established by Dr. Lowe and our board of directors, the achievement of which is evaluated by our Board of Directors). Pursuant to the terms of his severance agreement, Dr. Lowe will be entitled to severance benefits described in Termination or Change in Control Arrangements below.

Henry L. Hebel

Pursuant to an offer letter dated May 4, 2015, Mr. Hebel initially served as our Vice President of Operations and was appointed as our Vice President of Product Development in October 2015. Mr. Hebel's offer sets forth the principal terms and conditions of his employment, including his initial annual base salary of \$240,000, an annual target cash bonus opportunity of 25% of his base salary (which bonus is earned based on our achievement of specified milestones and performance objectives, as well as Mr. Hebel's performance relative to one or more performance objectives established by our board of directors, the achievement of which is evaluated by our Board of Directors). Mr. Hebel's offer letter provides for the grant of an option to purchase 33,442 shares of common stock under our 2015 Equity Incentive Plan. The option was granted with a per share exercise price determined to be not less than the fair market value of the shares on the date of grant and the right to purchase shares underlying the option vest over four years as described more fully in Outstanding Equity Awards at December 31, 2015 below. Mr. Hebel's offer letter also provides for the grant of an option to purchase 12,368 shares of common stock under our 2015 Equity Incentive Plan. The option was granted with a per share exercise price determined to be not less than the fair market value of the shares on the date of grant and the right to purchase shares underlying the option vest over five years as described more fully in Outstanding Equity Awards at December 31, 2015 below. Pursuant to the terms of his severance agreement, Mr. Hebel is entitled to severance benefits described in Termination or Change in Control Agreements below.

Scott W. Rowlinson, Ph.D.

Pursuant to an offer letter dated December 28, 2013, Dr. Rowlinson serves as our Vice President of Research & Development. Dr. Rowlinson's offer letter sets forth the principal terms and conditions of his employment, including his initial annual base salary of \$235,000, an annual target cash bonus opportunity of 20% of his base salary (which bonus is earned based on our achievement of specified milestones and performance objectives, as well as Dr. Rowlinson's performance relative to one or more performance objectives established by our board of directors, the achievement of which is evaluated by our Board of Directors). Dr. Rowlinson's offer letter provides for the grant of 22,109 Common B shares under our 2013 Equity Incentive Plan. The shares were granted with a threshold amount determined to be not less than the amount of distributions that would be distributed to the members in a liquidation and the shares vest over four years. In connection with the Conversion the Common B shares were converted into restricted common stock and options to purchase common stock, the vesting of which is described in more detail in Outstanding Equity Awards at December 31, 2015 below. Pursuant to the terms of his severance agreement, Dr. Rowlinson will be entitled to severance benefits described in Termination or Change in Control Arrangements below.

Table of Contents**Outstanding Equity Awards at December 31, 2015**

The following table presents, for our Named Executive Officers, information regarding outstanding equity awards held as of December 31, 2015.

Name	Option Awards (1)				Stock Awards	
	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 or units of stock that have not vested (\$)(2)
David G. Lowe, Ph.D.		19,654(3)	\$ 3.47	3/31/2025		
	19,652		3.47	3/31/2025		
	6,926					
		104,167(4)	3.47	3/31/2025		
		100,181(5)	3.47	3/31/2025		
					61,416(6)	614,160
Henry L. Hebel		33,442(7)	6.20	5/27/2025		
		12,368(8)	6.20	5/27/2025		
Scott W. Rowlinson, Ph.D.	2,345	3,015(9)	3.47	3/31/2025		
		27,822(4)	3.47	3/31/2025		
		18,784(5)	3.47	3/31/2025		
					9,422(10)	94,220

(1) All of the outstanding option awards were granted under our 2015 Equity Incentive Plan.

(2) The market price of our common stock is based on the initial public offering price of \$10.00 per share.

(3) These stock options vest as follows: 25% of the shares of common stock underlying the options vested on March 10, 2015, then 1/16th of the shares of common stock underlying the options vested on March 24, 2015 and thereafter 1/16th of the shares of common stock underlying the options vest at the end of each three month period elapsed.

(4) These stock options vest as follows: 25% of the shares of common stock underlying the options vest on March 20, 2016 and thereafter 1/16th of the shares of common stock underlying the options vest at the end of each three month period elapsed.

(5)

These stock options vest as follows: 25% of the shares of common stock underlying the options vest on March 20, 2017 and thereafter 1/16th of the shares of common stock underlying the options vest at the end of each three month period elapsed.

- (6) On the date of grant, 52,353 shares were vested and 92,124 shares were unvested. 1/16th of the shares vested on March 24, 2015 and 1/16th of the shares vest quarterly thereafter.
- (7) These stock options vest as follows: 25% of the shares of common stock underlying the options vest on May 26, 2016 and thereafter 1/16th of the shares of common stock underlying the options vest at the end of each three month period elapsed.
- (8) These stock options vest as follows: 25% of the shares of common stock underlying the options vest on May 26, 2017 and thereafter 1/16th of the shares of common stock underlying the options vest at the end of each three month period elapsed.
- (9) These stock options vest as follows: 25% of the shares of common stock underlying the options vested on March 10, 2015, then 1/16th of the shares of common stock underlying the option vested on May 18, 2015 and thereafter 1/16th of the shares shall vest at the end of each three month period elapsed.
- (10) On the date of grant, 4,187 shares were vested and 12,562 shares were unvested. 1/16th of the shares vested on May 18, 2015 and 1/16th of the shares vest quarterly thereafter.

Termination or Change in Control Arrangements

Pursuant to his severance agreement, if Dr. Lowe's employment is terminated for any reason other than for cause or Dr. Lowe voluntarily resigns his employment for good reason, we shall provide Dr. Lowe with: (i) continuation of his monthly base salary for up to 12 months following such separation and (ii) payment for the full amount of Dr. Lowe's premiums under the Consolidated Omnibus Budget Reconciliation Act or COBRA. Additionally, if Dr. Lowe's employment is terminated within 12 months of a change in control or within three months preceding a change in control for any reason other than for cause or Dr. Lowe voluntarily resigns his employment for good reason during such period, we will provide Dr. Lowe with severance payments consisting of: (i) his base salary for up to the following 12 months; (ii) 100% vesting for all outstanding and unvested stock options, restricted stock awards, restricted stock units and other stock based awards and (iii) payment for the full amount of Dr. Lowe's premiums under COBRA.

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Pursuant to their severance agreements, Mr. Hebel and Dr. Rowlinson will receive the following benefits if such Vice President's employment is terminated for any reason other than for cause or such Vice President voluntarily resigns his employment for good reason: (i) a severance amount equal to 12 weeks of base salary plus an additional two weeks of base salary for each full year of employment with us, up to a maximum benefit of six months of base salary and (ii) payment for the full amount of such Vice President's premiums under COBRA. Additionally, if such Vice President's employment is terminated within 12 months of a change in control or within three months preceding a change in control for any reason other than for cause or such Vice President voluntarily resigns his employment for good reason during such period, we will provide such Vice President with severance payments consisting of: (i) six months of his base salary; (ii) 100% vesting for all outstanding and unvested stock options, restricted stock awards, restricted stock units and other stock based awards and (iii) payment for the full amount of such Vice President's premiums under COBRA.

Employee Benefit and Stock Plans

2015 Equity Incentive Plan

Our 2015 Equity Incentive Plan was adopted by our board of directors and approved by our stockholders on March 10, 2015. The 2015 Equity Incentive Plan provides for the grant of both incentive stock options, which qualify for favorable tax treatment to their recipients under Section 422 of the Code, and nonstatutory stock options, as well as for the issuance of shares of restricted stock, stock appreciation rights and restricted stock units. We may grant incentive stock options only to our employees, including officers and directors who are also employees. We may grant nonstatutory stock options to our employees, officers, directors and consultants. The exercise price of each stock option must be at least equal to the fair market value of our common stock on the date of grant. The exercise price of incentive stock options granted to 10% stockholders must be at least equal to 110% of the fair market value of our common stock on the date of grant. The maximum permitted term of options granted under our 2015 Equity Incentive Plan is ten years, except that the maximum permitted term of incentive stock options granted to 10% stockholders is five years. In the event of our merger or consolidation, the 2015 Equity Incentive Plan provides that awards may be assumed, converted or replaced by the successor or acquiring entity. Unless as otherwise approved by our board of directors or required by the terms of any option agreement governing such options, all unexercised options shall terminate upon the consummation of the merger or consolidation if they are not assumed or substituted.

As of December 31, 2015, we had reserved 1,228,714 shares of our common stock for issuance under our 2015 Equity Incentive Plan. As of December 31, 2015, options to purchase 4,580 of these shares had been exercised, options to purchase 629,848 of these shares remained outstanding and 594,286 of these shares remained available for future grant. The options outstanding as of December 31, 2015 had a weighted-average exercise price of \$4.55 per share. We will cease issuing awards under our 2015 Equity Incentive Plan upon the implementation of our 2016 Equity Incentive Plan. We will not grant any additional options under the 2015 Equity Incentive Plan following the date of this prospectus, and the 2015 Equity Incentive Plan will terminate at that time. However, any outstanding options granted under the 2015 Equity Incentive Plan will remain outstanding, subject to the terms of our 2015 Equity Incentive Plan and stock option agreements, until such outstanding options are exercised or until they terminate or expire by their terms. As of December 31, 2015, no restricted stock awards, stock appreciation rights or restricted stock units have been granted under the 2015 Equity Incentive Plan but should any such awards be granted, they will have terms similar to those described below with respect to such awards to be granted under our 2016 Equity Incentive Plan.

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2016 Equity Incentive Plan

We have adopted a 2016 Equity Incentive Plan that became effective on the date immediately prior to the date of this prospectus and serves as the successor to our 2015 Equity Incentive Plan. We have reserved 1,100,000 shares of our common stock to be issued under our 2016 Equity Incentive Plan. The number of shares reserved for issuance under our 2016 Equity Incentive Plan will increase automatically on January 1 of each of 2017 through 2023 by the number of shares equal to 4% of the aggregate number of outstanding shares of our common stock as of the immediately preceding December 31. However, our board of directors may reduce the amount of the increase in any particular year. In addition, the following shares will again be available for grant and issuance under our 2016 Equity Incentive Plan:

- n shares subject to options or stock appreciation rights granted under our 2016 Equity Incentive Plan that cease to be subject to the option or stock appreciation right for any reason other than exercise of the option or stock appreciation right;
- n shares subject to awards granted under our 2016 Equity Incentive Plan that are subsequently forfeited or repurchased by us at the original issue price;
- n shares subject to awards granted under our 2016 Equity Incentive Plan that otherwise terminate without shares being issued;
- n shares surrendered, cancelled or exchanged for cash or a different award (or combination thereof);
- n shares of common stock reserved but not issued or subject to outstanding grants under our 2015 Equity Incentive Plan on the date of this prospectus will be available for grant and issuance under our 2016 Equity Incentive Plan;
- n shares of common stock issuable upon the exercise of options or subject to other awards under our 2015 Equity Incentive Plan prior to the date of this prospectus that cease to be subject to such options or other awards by forfeiture or otherwise after the date of this prospectus will be available for grant and issuance under our 2016 Equity Incentive Plan;
- n shares of common stock issued under our 2015 Equity Incentive Plan that are forfeited or repurchased by us after the date of this prospectus will be available for grant and issuance under our 2016 Equity Incentive Plan; and
- n shares of common stock subject to awards under our 2015 Equity Incentive Plan that are used to pay the exercise price of an option or withheld to satisfy the tax withholding obligations related to any award will be available for grant and issuance under our 2016 Equity Incentive Plan.

Our 2016 Equity Incentive Plan authorizes the award of stock options, restricted stock awards (RSAs), stock appreciation rights (SARs), restricted stock units (RSUs), performance awards and stock bonuses. No person is eligible to receive more than 400,000 shares in any calendar year under our 2016 Equity Incentive Plan other than a new employee of ours, who is eligible to receive no more than 775,000 shares under the plan in the calendar year in which the employee commences employment. No more than 5,500,000 shares will be issued pursuant to the exercise of incentive stock options. No non-employee member of our board will be eligible to receive more than 100,000 shares in any calendar year under our 2016 Equity Incentive Plan.

Our 2016 Equity Incentive Plan is administered by our compensation committee, all of the members of which are outside directors as defined under applicable federal tax laws, or by our board of directors acting in place of our compensation committee. The compensation committee has the authority to construe and interpret our 2016 Equity Incentive Plan, grant awards and make all other determinations necessary or advisable for the administration of the plan.

Our 2016 Equity Incentive Plan provides for the grant of awards to our employees, directors, consultants, independent contractors and advisors, provided the consultants, independent contractors,

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directors and advisors are natural persons that render services not in connection with the offer and sale of securities in a capital-raising transaction. The exercise price of stock options must be at least equal to the fair market value of our common stock on the date of grant.

We anticipate that in general, options will vest over a four-year period. Options may vest based on time or achievement of performance conditions. Our compensation committee may provide for options to be exercised only as they vest or to be immediately exercisable with any shares issued on exercise being subject to our right of repurchase that lapses as the shares vest. The maximum term of options granted under our 2016 Equity Incentive Plan is ten years.

An RSA is a grant by us of shares of our common stock subject to restrictions, which may vest based on time or achievement of performance conditions. The price (if any) of an RSA will be determined by the compensation committee. Unless otherwise determined by the compensation committee at the time of award, vesting will cease on the date the participant no longer provides services to us and unvested shares will be forfeited to or repurchased by us.

SARs provide for a payment, or payments, in cash or shares of our common stock, to the holder based upon the difference between the fair market value of our common stock on the date of exercise and the stated exercise price up to a maximum amount of cash or number of shares. SARs may vest based on time or achievement of performance conditions.

RSUs represent the right to receive shares of our common stock at a specified date in the future, subject to forfeiture of that right because of termination of employment or failure to achieve certain performance conditions. If an RSU has not been forfeited, then on the date specified in the RSU agreement, we will deliver to the holder of the restricted stock unit whole shares of our common stock (which may be subject to additional restrictions), cash or a combination of our common stock and cash.

Performance shares are performance awards that cover a number of shares of our common stock that may be settled upon achievement of the pre-established performance conditions in cash or by issuance of the underlying shares. These awards are subject to forfeiture prior to settlement because of termination of employment or failure to achieve the performance conditions. No participant is eligible to receive more than \$10,000,000 in performance awards in any calendar year.

Stock bonuses may be granted as additional compensation for service or performance and, therefore, will not be issued in exchange for cash.

In the event there is a specified type of change in our capital structure without our receipt of consideration, such as a stock split, appropriate adjustments will be made to the number of shares reserved under our 2016 Equity Incentive Plan, the maximum number of shares that can be granted in a calendar year and the number of shares and exercise price, if applicable, of all outstanding awards under our 2016 Equity Incentive Plan.

Awards granted under our 2016 Equity Incentive Plan may not be transferred in any manner other than by will or by the laws of descent and distribution or as determined by our compensation committee. Unless otherwise permitted by our compensation committee, stock options may be exercised during the lifetime of the optionee only by the optionee or the optionee's guardian or legal representative. Options granted under our 2016 Equity Incentive Plan generally may be exercised for a period of three months after the termination of the optionee's service to us, for a period of 12 months in the case of death or disability, or such longer period as our compensation committee may provide. Options generally terminate immediately upon termination of employment for cause.

Our 2016 Equity Incentive Plan provides that, in the event of specified types of mergers or consolidations, a sale, lease, or other disposition of all or substantially all of our assets or a corporate

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transaction, outstanding awards under our 2016 Equity Incentive Plan may be assumed or replaced by any surviving or acquiring corporation; the surviving or acquiring corporation may substitute similar awards for those outstanding under our 2016 Equity Incentive Plan; outstanding awards may be settled for the full value of such outstanding award (whether or not then vested or exercisable) in cash, cash equivalents, or securities (or a combination thereof) of the successor entity with payment deferred until the date or dates the award would have become exercisable or vested; or outstanding awards may be terminated for no consideration. Our board of directors or its compensation committee has the discretion to provide that a stock award under our 2016 Equity Incentive Plan will immediately vest as to all or any portion of the shares subject to the stock award at the time of a corporate transaction or in the event a participant's service with us or a successor entity is terminated actually or constructively within a designated period following the occurrence of the transaction. Stock awards held by participants under our 2016 Equity Incentive Plan will not vest automatically on such an accelerated basis unless specifically provided in the participant's applicable award agreement. In the event of a corporate transaction, the vesting of all awards granted to non-employee directors shall accelerate and such awards shall become exercisable (as applicable) in full upon the consummation of the corporate transaction.

Our 2016 Equity Incentive Plan will terminate ten years from the date our board of directors adopts the plan, unless it is terminated earlier by our board of directors. Our board of directors may amend or terminate our 2016 Equity Incentive Plan at any time. Our board of directors generally may amend our 2016 Equity Incentive Plan, without stockholder approval unless required by applicable law.

2016 Employee Stock Purchase Plan

We have adopted a 2016 Employee Stock Purchase Plan in order to enable eligible employees to purchase shares of our common stock at a discount following the date of this offering. Purchases will be accomplished through participation in discrete offering periods. Our 2016 Employee Stock Purchase Plan is intended to qualify as an employee stock purchase plan under Section 423 of the Code. We reserved 165,000 shares of our common stock for issuance under our 2016 Employee Stock Purchase Plan.

Our compensation committee will administer our 2016 Employee Stock Purchase Plan. Our employees generally are eligible to participate in our 2016 Employee Stock Purchase Plan; our compensation committee may in its discretion elect to exclude employees who work less than 20 hours per week or less than five months in a calendar year. Employees who are 5% stockholders, or would become 5% stockholders as a result of their participation in our 2016 Employee Stock Purchase Plan, are ineligible to participate in our 2016 Employee Stock Purchase Plan. We may impose additional restrictions on eligibility. Under our 2016 Employee Stock Purchase Plan, eligible employees will be able to acquire shares of our common stock by accumulating funds through payroll deductions. Our eligible employees will be able to select a rate of payroll deduction between 1% and 15% of their base cash compensation. We will also have the right to amend or terminate our 2016 Employee Stock Purchase Plan at any time. Our 2016 Employee Stock Purchase Plan will terminate on the tenth anniversary of the last day of the first purchase period, unless it is terminated earlier by our board of directors.

When an initial purchase period commences, our employees who meet the eligibility requirements for participation in that purchase period will automatically be granted a nontransferable option to purchase shares in that purchase period. For subsequent purchase periods, new participants will be required to enroll in a timely manner. Once an employee is enrolled, participation will be automatic in subsequent purchase periods. An employee's participation automatically ends upon termination of employment for any reason.

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The first offering period will begin on a date approved by our board of directors or compensation committee. Each subsequent purchase period will be for six months (commencing each February 16 and August 16).

No participant will have the right to purchase our shares in an amount, when aggregated with purchase rights under all our employee stock purchase plans that are also in effect in the same calendar year(s), that has a fair market value of more than \$50,000, determined as of the first day of the applicable purchase period, for each calendar year in which that right is outstanding. In addition, no participant will be permitted to purchase more than 2,000 shares during any one purchase period or such lesser amount determined by our compensation committee. The purchase price for shares of our common stock purchased under our 2016 Employee Stock Purchase Plan will be 85% of the lesser of the fair market value of our common stock on (i) the first trading day of the applicable offering period and (ii) the last trading day of each purchase period in the applicable offering period.

If we experience a change in control transaction, any offering period that commenced prior to the closing of the proposed change in control transaction will be shortened and terminated on a new purchase date. The new purchase date will occur prior to the closing of the proposed change in control transaction and our 2016 Employee Stock Purchase Plan will then terminate on the closing of the proposed change in control.

Our 2016 Employee Stock Purchase Plan will terminate ten years from the first purchase date under the plan, unless it is terminated earlier by our board of directors. Our board of directors may amend or terminate our 2016 Employee Stock Purchase Plan at any time. Our board of directors generally may amend our 2016 Employee Stock Purchase Plan, without stockholder approval unless required by applicable law.

Non-Employee Director Compensation

The following table presents the total compensation earned in the year ended December 31, 2015 for each member of our board of directors, except for our Chief Executive Officer, Dr. Lowe, who receives no additional compensation for his service as a director and Dr. Quinn, who joined our board of directors in March 2016. Other than as described in the table below, none of our directors, except Dr. Lowe, received fees or reimbursement of any expenses (other than customary expenses in connection with the attendance of meetings of our board of directors) or any equity or non-equity awards in the year ended December 31, 2015.

Name of Director	Fees Earned or Paid in Cash (\$)	Option Awards (\$)(1)	All Other Compensation (\$)	Total (\$)
Armen Shanafelt, Ph.D.				
Henry Skinner, Ph.D.				
George Georgiou, Ph.D.			50,000(2)	50,000
Sandesh Mahatme	17,500	217,250		234,750
Russell J. Cox	17,500	217,250		234,750

- (1) The amounts reported in this column represent the aggregate grant date fair value of the awards granted to our non-employee directors during the year ended December 31, 2015, as computed in accordance with Accounting Standards Codification Topic 718. The assumptions used in calculating the grant date fair value of the awards reported in the Option Awards column are set forth in Note 9 of our Notes to Consolidated Financial Statements. Note that the amounts reported in this column reflect the aggregate accounting cost for these awards, and do not necessarily correspond to the actual economic value that may be received by the non-employee directors from the

awards. For information regarding the number of stock options and restricted common stock held by each non-employee director as of December 31, 2015, see the table below.

- (2) Represents consulting fees paid to Dr. Georgiou in connection with research services provided pursuant to a consulting agreement between Dr. Georgiou and us.

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Our non-employee directors held the following number of stock options and restricted common stock as of December 31, 2015.

	Outstanding Stock Awards (#)	Shares subject to Outstanding Options (#)
Armen Shanafelt, Ph.D.		
Henry Skinner, Ph.D.		
George Georgiou, Ph.D.	43,290(1)	13,852(1)
Sandesh Mahatme		23,809
Russell J. Cox		23,809

(1) Represents restricted common stock and stock options issued to Dr. Georgiou in connection with research services provided pursuant to a consulting agreement between Dr. Georgiou and us.

In June 2015, we adopted a non-employee director compensation program that will be effective upon the completion of this offering. Under this program, each new, non-employee director who joins our board of directors will be granted equity compensation (in the form of stock options) upon the effective date of his or her election to our board of directors with a fair value (calculated in accordance with Accounting Standards Codification Topic 718) at the time of grant equal to \$300,000, with an annual equity grant with a fair value (calculated in accordance with Accounting Standards Codification Topic 718) at the time of grant equal to \$100,000. Equity awards for new directors will vest in equal monthly installments for three years after the grant date if the director has served continuously as a member of our board of directors through the applicable vesting date. Annual equity grants for directors will vest in equal monthly installments for one year after the grant date if the director has served continuously as a member of our board of directors through the applicable vesting date. In addition, equity awards for new directors will vest in full in the event that we are subject to a change in control or upon certain other events.

The chairman of the board is entitled to receive an annual cash retainer of \$25,000 for his or her service on the board of directors, additionally non-employee members of the board of directors receive annual cash retainers of \$35,000. Non-employee directors serving on committees are also eligible to receive cash retainers for their service. The chair of the audit committee will receive an annual cash retainer of \$15,000, while members of the committee receive annual cash retainers of \$7,500. The chair of the compensation committee will receive an annual cash retainer of \$10,000, while members of the committee receive annual cash retainers of \$5,000. The chair of the nominating and governance committee will receive an \$8,000 cash retainer, and members will receive annual cash retainers of \$4,000.

Limitations on Liability and Indemnification Matters

Our restated certificate of incorporation that will become effective in connection with the closing of this offering contains provisions that limit the liability of our directors for monetary damages to the fullest extent permitted by the Delaware General Corporation Law. Consequently, our directors will not be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duties as directors, except liability for:

- n any breach of the director's duty of loyalty to us or our stockholders;
- n any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- n

unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law; or

n any transaction from which the director derived an improper personal benefit.

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Our restated certificate of incorporation and our restated bylaws that will become effective in connection with the closing of this offering require us to indemnify our directors and officers to the maximum extent not prohibited by the Delaware General Corporation Law and allow us to indemnify other employees and agents as set forth in the Delaware General Corporation Law. Subject to certain limitations, our restated bylaws also require us to advance expenses incurred by our directors and officers for the defense of any action for which indemnification is required or permitted.

We have entered, and intend to continue to enter, into separate indemnification agreements with our directors, officers and certain of our key employees, in addition to the indemnification provided for in our restated certificate of incorporation and restated bylaws. These agreements, among other things, require us to indemnify our directors, officers and key employees for certain expenses, including attorneys' fees, judgments, penalties, fines and settlement amounts actually incurred by these individuals in any action or proceeding arising out of their service to us or any of our subsidiaries or any other company or enterprise to which these individuals provide services at our request. Subject to certain limitations, our indemnification agreements also require us to advance expenses incurred by our directors, officers and key employees for the defense of any action for which indemnification is required or permitted.

We believe that these indemnification provisions and agreements are necessary to attract and retain qualified directors, officers and key employees. We also maintain directors' and officers' liability insurance.

The limitation of liability and indemnification provisions in our restated certificate of incorporation and restated bylaws may discourage stockholders from bringing a lawsuit against our directors and officers for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and other stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damage awards against directors and officers as required by these indemnification provisions.

At present, there is no pending litigation or proceeding involving any of our directors or executive officers as to which indemnification is required or permitted, and we are not aware of any threatened litigation or proceeding that may result in a claim for indemnification.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, executive officers or persons controlling us, we have been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Table of Contents**CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS**

We describe below transactions and series of similar transactions, since our inception on December 16, 2013, to which we were a party or will be a party, in which:

- n the amounts involved exceeded or will exceed \$120,000; and
- n any of our directors, executive officers, promoters or holders of more than 5% of our capital stock, or any affiliate or immediate family member of, or person sharing the household with, any of these individuals, had or will have a direct or indirect material interest.

Other than as described below, there have not been, nor are there any currently proposed, transactions or series of similar transactions to which we have been or will be a party other than compensation arrangements, which are described where required under Executive Compensation.

Equity Financings***Series A convertible preferred share financing***

In December 2013, we sold an aggregate of 971,928 shares of our Series A convertible preferred shares to investors at a purchase price of \$5.25 per share, for an aggregate purchase price of \$5,102,632. This included an aggregate of 952,380 Series A convertible preferred shares sold to Novartis Bioventures Ltd. and Lilly Ventures Fund I LLC for an aggregate purchase price of \$5,000,000. Novartis Bioventures Ltd. and Lilly Ventures Fund I LLC each agreed to purchase additional Series A convertible preferred shares in a second tranche closing in the event that we reached certain agreed-upon milestones. In July 2014, we sold an additional aggregate of 1,067,592 shares of our Series A convertible preferred shares in a second tranche at a purchase price of \$5.25 per share, for an aggregate purchase price of \$5,604,868. As part of this second tranche, we sold an aggregate of 851,429 Series A convertible preferred shares in a second tranche closing to Novartis Bioventures Ltd., Lilly Ventures Fund I LLC and Joseph E. Tyler, for an aggregate purchase price of \$4,470,000. The table below sets forth the aggregate number of shares of Series A convertible preferred shares sold to our directors, executive officers or holders of more than 5% of our capital stock: On March 10, 2015, these Series A convertible preferred shares were converted 1:1 into shares of Series A convertible preferred stock.

Name of Stockholder	Series A	Series A	Total Purchase Price (\$)
	Convertible Preferred	Convertible Preferred Shares	
	Shares Issued in December	Issued at July 2014	
	2013	Second Tranche Closing	
Lilly Ventures Fund I LLC(1)	476,190	414,286	4,675,000
Novartis Bioventures Ltd.(2)	476,190	414,286	4,675,000
Joseph E. Tyler(3)		22,857	120,000

(1) Lilly Ventures Fund I, LLC beneficially owns more than 5% of our capital stock. Dr. Armen Shanafelt, a member of our board of directors, is a General Partner of LV Management Group, LLC. LV Management Group, LLC is the management company for Lilly Ventures Fund I, LLC.

- (2) Novartis Bioventures Ltd. beneficially owns more than 5% of our capital stock. Dr. Henry Skinner is an employee of a corporation that is affiliated with Novartis Bioventures Ltd. Dr. Skinner resigned from our board of directors effective immediately prior to the effectiveness of the registration statement of which this prospectus forms a part.
- (3) Mr. Tyler is our Vice President, Manufacturing.
- The purchasers of our Series A convertible preferred stock are entitled to specified registration rights. For additional information, see Description of Capital Stock Registration Rights.

Series B convertible preferred stock financing

In March 2015, we sold an aggregate of 4,929,948 shares of our Series B convertible preferred stock to investors for an aggregate purchase price of \$44,000,000. As part of this financing, we sold an

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aggregate of 3,249,299 shares of Series B convertible preferred stock to Novartis Bioventures Ltd., Lilly Ventures Fund I LLC, OrbiMed Private Investments V, LP and Jennison Global Healthcare Master Fund Ltd at a purchase price of \$8.93 per share for an aggregate purchase price of \$29,000,000. The following table summarizes the Series B convertible preferred stock sold to our directors, executive officers or holders of more than 5% of our capital stock:

Name of Stockholder	Shares of Series B convertible preferred stock	Total Purchase Price (\$)
Jennison Global Healthcare Master Fund Ltd.(1)	448,179	4,000,000
Lilly Ventures Fund I LLC(2)	1,120,448	10,000,000
Novartis Bioventures Ltd.(3)	1,120,448	10,000,000
OrbiMed Private Investments V, LP(4)	560,224	5,000,000

- (1) Jennison Global Healthcare Master Fund, Ltd. beneficially owns more than 5% of our capital stock.
- (2) Lilly Ventures Fund I LLC beneficially owns more than 5% of our capital stock. Dr. Armen Shanafelt, a member of our board of directors, is a General Partner of LV Management Group, LLC. LV Management Group, LLC is the management company for Lilly Ventures Fund I, LLC.
- (3) Novartis Bioventures Ltd. beneficially owns more than 5% of our capital stock. Dr. Henry Skinner is an employee of a corporation that is affiliated with Novartis Bioventures Ltd. Dr. Skinner resigned from our board of directors effective immediately prior to the effectiveness of the registration statement of which this prospectus forms a part.
- (4) OrbiMed Private Investments V, L.P. beneficially owns more than 5% of our capital stock.
- The purchasers of our Series B convertible preferred stock are entitled to specified registration rights. For additional information, see Description of Capital Stock Registration Rights.

Consulting Agreement with Ann M. Lowe, M.D.

On December 24, 2013, we entered into a consulting agreement with Dr. Ann M. Lowe, the wife of our Chief Executive Officer and President. Dr. Ann Lowe agreed to provide clinical research and consulting services to us at a rate of \$375 per hour, and to perform up to 20 hours of services per week. Under the consulting agreement, we paid Dr. Ann Lowe \$146,000 and \$433,000 in 2014 and 2015, respectively. We also agreed to indemnify Dr. Ann Lowe from any losses she may incur arising out of any product liability theory arising from a drug or service provided by us. The agreement contains confidentiality and invention-assignment provisions. The agreement has no specific term and either party may terminate the agreement upon providing written notice.

Consulting Agreement with George Georgiou, Ph.D.

On February 18, 2014, we entered into a consulting agreement with Dr. Georgiou, who is one of our founders, directors and beneficial owner of more than 5% of our capital stock. Dr. Georgiou agreed to provide analysis and feedback on grant applications, research and development plans, and results arising from such plans for Arginase, Cystinase and Methioninase or other molecules that may be licensed by us or our affiliates from the University of Texas at Austin. He also agreed to attend meetings and make presentations for our future fundraising efforts, and to provide services related to our applications for certain grants. The agreement contains confidentiality and invention-assignment provisions.

Pursuant to this agreement, we agreed to pay Dr. Georgiou \$50,000 per year and issue him 57,142 shares of our Common B shares, subject to vesting contingent on the achievement of certain performance milestones. In 2014, we

paid Dr. Georgiou \$50,000 and issued him 57,142 Common B shares, subject to the vesting conditions. In 2015, we paid Dr. Georgiou \$50,000.

The consulting agreement has a term of four years, subject to automatic renewal for additional one month periods thereafter until terminated. Either party may terminate the agreement upon providing written notice.

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Assignment of Intellectual Property from George Georgiou, Ph.D.

In December 2013, we acquired in-process research and development assets from GMA Technologies, L.L.C., or GMA. Dr. Georgiou is the manager of GMA. GMA agreed to assign, convey, transfer and deliver to us all of its rights, title and interest in certain patents and patent applications and all of the know-how owned by GMA related to or used in connection with such patents and patent applications, including certain proprietary information, ideas, inventions, trade secrets, techniques and designs. The patents and patent rights assigned by GMA provide us with full right, title and interest in three families of patents and patent rights: (i) compositions of engineered human arginases and methods for treating cancer (ii) methods for purifying pegylated arginase and (iii) engineered enzymes with methionine-gamma-lyase enzymes and pharmacological preparations of such enzymes. These patents and patent rights include cell lines and expression constructs for production of recombinantly produced enzymes that are our lead product candidates.

Concurrently, we agreed to issue GMA 165,000 Common A-1 shares, and 200,714 Common A shares to Dr. Georgiou, which were issued in 2013. On March 10, 2015, the shares issued to GMA were converted into 165,000 shares of common stock and the shares issued to Dr. Georgiou were converted into 200,714 shares of common stock. Additionally, we promised to reimburse GMA up to \$250,000 for intellectual property expenses paid prior to our formation and legal fees that GMA incurred in connection with our formation plus 8% interest per annum.

Amended and Restated Investors Rights Agreement

We have entered into an amended and restated investors rights agreement with holders of our convertible preferred stock, including Dr. Lowe, our President, Chief Executive Officer and member of our board of directors; Mr. York, our Chief Financial Officer; Mr. Tyler, our Vice President of Manufacturing; Dr. Rowlinson, our Vice President of Research; and Dr. Georgiou, one of our founders, directors and beneficial owner of more than 5% of our capital stock, entities with which certain of our directors are affiliated and our other principal stockholders. These stockholders are entitled to rights with respect to the registration of their shares following our initial public offering under the Securities Act. For a description of these registration rights, see Description of Capital Stock Registration Rights.

Indemnification Agreements

We have entered into indemnification agreements with each of our directors and executive officers. The indemnification agreements and our restated certificate of incorporation and our restated bylaws to be in effect upon completion of this offering will require us to indemnify our directors to the fullest extent not prohibited by Delaware law. Subject to certain limitations, our restated bylaws also require us to advance expenses incurred by our directors and officers. For more information regarding these agreements, see Executive Compensation Limitations on Liability and Indemnification Matters.

Insider Participation

Certain of our existing stockholders or their affiliates have agreed to purchase an aggregate of approximately 3,175,000 shares of our common stock in this offering at the initial public offering price. The underwriters will receive the same underwriting discount on the shares purchased by these parties as they will on the other shares sold to the public in this offering.

Policies and Procedures for Related Party Transactions

In connection with this offering we have adopted a written related person transactions policy that our executive officers, directors, nominees for election as a director, beneficial owners of more than 5% of our common stock, and any members of the immediate family of and any entity affiliated with any of the foregoing persons, are not permitted to enter into a material related person transaction with us

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without the review and approval of our audit committee, or a committee composed solely of independent directors in the event it is inappropriate for our audit committee to review such transaction due to a conflict of interest. The policy provides that any request for us to enter into a transaction with an executive officer, director, nominee for election as a director, beneficial owner of more than 5% of our common stock or with any of their immediate family members or affiliates in which the amount involved exceeds \$120,000 will be presented to our audit committee for review, consideration and approval. In approving or rejecting any such proposal, our audit committee will consider the relevant facts and circumstances available and deemed relevant to the audit committee, including, but not limited to, whether the transaction is on terms no less favorable than terms generally available to an unaffiliated third party under the same or similar circumstances and the extent of the related person's interest in the transaction.

Although we have previously not had a written policy for the review and approval of transactions with related persons, our board of directors has historically reviewed and approved any transaction where a director or officer had a financial interest, including the transactions described above. Prior to approving such a transaction, the material facts as to a director's or officer's relationship or interest in the agreement or transaction were disclosed to our board of directors. Our board of directors took this information into account when evaluating the transaction and in determining whether such transaction was fair to the company and in the best interest of all of our stockholders.

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PRINCIPAL STOCKHOLDERS

The following table sets forth certain information with respect to the beneficial ownership of our common stock at February 29, 2016, and as adjusted to reflect the sale of common stock in this offering, for:

- n each of our directors;
- n each of our named executive officers;
- n all of our current directors and executive officers as a group; and
- n each person, or group of affiliated persons, who beneficially owned more than 5% of our common stock.

We have determined beneficial ownership in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Except as indicated by the footnotes below, we believe, based on information furnished to us, that the persons and entities named in the table below have sole voting and sole investment power with respect to all shares of common stock that they beneficially owned, subject to applicable community property laws.

Applicable percentage ownership is based on 7,929,832 shares of common stock outstanding, on a pro forma basis, as of December 31, 2015 and assumes the conversion of all outstanding shares of preferred stock into an aggregate of 7,172,496 shares of our common stock. The applicable percentage ownership after this offering includes 5,000,000 shares of common stock that will be issued by us in our initial public offering (assuming no exercise of the underwriters' option to purchase additional shares of common stock). In computing the number of shares of common stock beneficially owned by a person and the percentage ownership of that person, we deemed to be outstanding all shares of common stock subject to options held by that person or entity that are currently exercisable or that will become exercisable within 60 days of February 29, 2016. We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other person. Unless otherwise indicated, the address of each beneficial owner listed in the table below is c/o Aeglea BioTherapeutics, Inc. 901 S. MoPac Expressway, Barton Oaks Plaza One, Suite 250, Austin, Texas 78746.

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At our request, the underwriters have reserved up to 5% of the common stock being offered by this prospectus for sale at the initial public offering price to our directors, officers, employees and other individuals associated with us and members of their families through a directed share program. In addition, certain of our existing stockholders or their affiliates have agreed to purchase an aggregate of approximately 3,175,000 shares of our common stock in this offering at the initial public offering price. The following table does not reflect the purchases by these parties.

Name of Beneficial Owner	Beneficial Ownership Prior to this Offering		Beneficial Ownership After this Offering	
	Number	Percent	Number	Percent
5% Stockholders:				
Lilly Ventures Fund I, LLC(1)	2,068,543	26.1%	2,068,543	16.0%
Novartis Bioventures Ltd.(2)	2,010,924	25.4%	2,010,924	15.6%
OrbiMed Private Investments V, LP(3)	560,224	7.1%	560,224	4.3%
Jennison Global Healthcare Master Fund(4)	448,179	5.7%	448,179	3.5%
Directors and Named Executive Officers:				
David G. Lowe, Ph.D.(5)	267,116	3.3%	267,116	2.1%
Scott W. Rowlinson, Ph.D.(6)	37,588	*	37,588	*
Henry L. Hebel		*		*
Armen Shanafelt, Ph.D.(1)	2,068,543	26.1%	2,068,543	16.0%
Henry Skinner, Ph.D.(7)		*		*
George Georgiou, Ph.D.(8)	416,230	5.2%	416,230	3.2%
Sandesh Mahatme(9)	6,613	*	6,613	*
Russell J. Cox(10)	6,613	*	6,613	*
Anthony G. Quinn M.B Ch.B, Ph.D.(11)		*		*
All executive officers and directors as a group (11 persons)(12)	2,882,182	35.9%	2,882,182	22.1%

* Represents beneficial ownership of less than one percent.

- (1) Represents shares of common stock held of record and beneficially by Lilly Ventures Fund I, LLC (LVFI). LV Management Group, LLC (LVMG) is the management company for LVFI and as such may be deemed to indirectly beneficially own the shares held by LVFI. Ed Torres is the sole member of LVMG and therefore may be deemed to beneficially own the shares beneficially owned by LVFI. The individual members (collectively, the Members) of LVFI are Ed Torres, Steve Hall, Armen Shanafelt and Eli Lilly and Company. The Members share voting and dispositive power with regard to the shares directly held by the LVFI. The Members disclaim beneficial ownership over such shares, except to the extent of any pecuniary interest therein. The mailing addresses of the beneficial owners are 115 West Washington Street, Suite 1680-South, Indianapolis, IN 46204.
- (2) Represents shares of common 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. Dr. Henry Skinner, a member of our board of directors, is also an employee of a corporation that is affiliated with Novartis Bioventures Ltd. Dr. Skinner disclaims beneficial ownership of the shares held by Novartis Bioventures Ltd., except to the extent of his pecuniary interest arising as a result of his employment by such affiliate of Novartis Bioventures Ltd. Novartis Bioventures

Ltd. is an indirectly owned subsidiary of Novartis AG. The address of Novartis Bioventures Ltd. is 131 Front Street, Hamilton, HM 12, Bermuda.

- (3) Represents shares of common stock held by OrbiMed Private Investment V, LP (OPI V). OrbiMed Capital GP V LLC (GP V) is the sole general partner of OPI V and as such may be deemed to indirectly beneficially own the shares held by OPI V. OrbiMed Advisors LLC (OrbiMed) pursuant to its authority as the sole managing member of GP V may be deemed to indirectly beneficially own the shares held by OPI V. Samuel D. Isaly is the managing member of and owner of a controlling interest in OrbiMed. Accordingly, OrbiMed and Mr. Isaly may be deemed to have voting and investment power over the shares held by OPI V. Each of GP V, OrbiMed and Mr. Isaly disclaim beneficial ownership with respect to such shares, except to the extent of their pecuniary interest therein, if any. The address of OPI V is 601 Lexington Avenue, 54th Floor, New York, NY 10022.
- (4) Represents shares of common stock held by Jennison Global Healthcare Master Fund, Ltd (the Jennison Fund). Jennison Associates LLC (Jennison Associates) as the investment manager of the Jennison Fund, has investment power and voting power over the shares owned by the Jennison Fund and may be deemed to beneficially own the shares held by the

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Jennison Fund. Jennison Associates expressly disclaims ownership of such shares, except to the extent of its pecuniary interest therein, if any. Jennison Associates is an indirect wholly-owned subsidiary of Prudential Financial, Inc., which is a publicly traded financial services firm. The Jennison Fund is an exempted investment company incorporated under the laws of the Cayman Islands. By virtue of his position with Jennison Associates, David Chan, Managing Director of Jennison and portfolio manager to the Jennison Fund, has authority to vote or dispose of the securities held by the Jennison Fund. David Chan expressly disclaims beneficial interest of such shares, except to the extent of his pecuniary interest therein, if any. The address of the Jennison Fund is c.o Jennison Associates LLC, 466 Lexington Avenue, New York, NY 10017.

- (5) Represents (i) 5,658 shares of common stock held by a family trust of which Dr. Lowe and his spouse are co-trustees, (ii) 206,382 shares of common stock held by Dr. Lowe and (iii) options exercisable for 55,076 shares of common within 60 days of February 29, 2016. Dr. Lowe's spouse, Dr. Ann M. Lowe, provides consulting services to us and may be deemed to be a beneficial owner of such shares.
- (6) Represents (i) 11,204 shares of common stock held by a family trust of which Dr. Rowlinson and his spouse are co-trustees, (ii) 16,749 shares of common stock held by Dr. Rowlinson and (iii) options exercisable for 9,635 shares of common within 60 days of February 29, 2016.
- (7) Novartis BioVentures Ltd. holds 2,010,924 shares of common stock. Dr. Henry Skinner, a member of our board of directors, is an employee of a corporation that is affiliated with Novartis Bioventures Ltd. Dr. Skinner does not have voting or dispositive power with regard to these shares.
- (8) Represents (i) 105,476 shares of common stock held by a family trust of which Dr. Georgiou and his spouse are co-trustees, (ii) 138,528 shares of common stock held by Dr. Georgiou, (iii) 165,000 shares of common stock held by GMA Technologies L.L.C (GMA) and (iv) options exercisable for 7,226 shares of common within 60 days of February 29, 2016. Dr. Georgiou is the manager of GMA and therefore may be deemed to beneficially own the shares held by GMA. Dr. Georgiou, as manager of GMA, and pursuant to the provisions of the limited liability company agreement of GMA, has voting and dispositive authority with respect to the shares owned by GMA. The mailing address of the beneficial owners are: GMA Technologies L.L.C., 6405 Williams Ridge Way, Austin, TX 78731 and Dr. Georgiou, 6405 Williams Ridge Way, Austin, TX 78731.
- (9) Represents options exercisable for 6,613 shares of common stock within 60 days of February 29, 2016.
- (10) Represents options exercisable for 6,613 shares of common stock within 60 days of February 29, 2016.
- (11) Dr. Quinn joined our Board of Directors in March 2016. On March 18, 2016, Dr. Quinn was granted an option to purchase 23,809 shares of our common stock, of which 661 shares are exercisable within 60 days of February 29, 2016.
- (12) Represents (i) 2,780,356 shares of common stock and (ii) options exercisable for 101,826 shares of common within 60 days of February 29, 2016.

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DESCRIPTION OF CAPITAL STOCK

Upon the closing of this offering, our authorized capital stock will consist of 500,000,000 shares of common stock, \$0.0001 par value per share, and 10,000,000 shares of undesignated preferred stock, \$0.0001 par value per share. The following description summarizes the most important terms of our capital stock. Because it is only a summary, it does not contain all the information that may be important to you. For a complete description, you should refer to our restated certificate of incorporation and restated bylaws to be in effect upon the closing of this offering, which are included as exhibits to the registration statement of which this prospectus forms a part, and to the applicable provisions of Delaware law.

Pursuant to the provisions of our current certificate of incorporation all of the outstanding convertible preferred stock will automatically convert into common stock in connection with the completion of this offering. On a pro forma basis, assuming the effectiveness of this conversion as of December 31, 2015 there were 7,929,832 shares of our common stock issued, held by approximately 64 stockholders of record, and no shares of our preferred stock outstanding. Our board of directors is authorized, without stockholder approval, to issue additional shares of our capital stock.

Common Stock

Dividend rights

Subject to preferences that may apply to any shares of preferred stock outstanding at the time, the holders of our common stock are entitled to receive dividends out of funds legally available if our board of directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that our board of directors may determine. See *Dividend Policy* above.

Voting rights

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders. We have not provided for cumulative voting for the election of directors in our restated certificate of incorporation. Accordingly, pursuant to our restated certificate of incorporation that will be in effect upon the completion of this offering, holders of a majority of the shares of our common stock will be able to elect all of our directors. Our restated certificate of incorporation establishes a classified board of directors, to be divided into three classes with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms.

No preemptive or similar rights

Our common stock is not entitled to preemptive rights, and is not subject to conversion, redemption or sinking fund provisions.

Right to receive liquidation distributions

Upon our liquidation, dissolution or winding-up, the assets legally available for distribution to our stockholders would be distributable ratably among the holders of our common stock and any participating preferred stock outstanding at that time, subject to prior satisfaction of all outstanding debt and liabilities and the preferential rights of and the payment of liquidation preferences, if any, on any outstanding shares of preferred stock.

Preferred Stock

Pursuant to the provisions of our current certificate of incorporation, all of our outstanding convertible preferred stock will automatically convert into common stock, with such conversion to be

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effective in connection with the completion of this offering. All series of convertible preferred stock will convert at a ratio of one share of common stock for each share of convertible preferred stock.

Following this offering, our board of directors will be authorized, subject to limitations prescribed by Delaware law, to issue preferred stock in one or more series, to establish from time to time the number of shares to be included in each series and to fix the designation, powers, preferences and rights of the shares of each series and any of their qualifications, limitations or restrictions, in each case without further vote or action by our stockholders. Our board of directors can also increase or decrease the number of shares of any series of preferred stock, but not below the number of shares of that series then outstanding, without any further vote or action by our stockholders. 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 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 our company and might adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock. We have no current plan to issue any shares of preferred stock.

Options

As of December 31, 2015, we had outstanding options to purchase an aggregate 629,848 shares of our common stock, with a weighted-average exercise price of \$4.55. Additional options to purchase 84,417 shares of our common stock, with an exercise price of \$5.46, have been granted since January 1, 2016.

Registration Rights

Pursuant to the terms of our investors' rights agreement, immediately following this offering, the holders of 7,230,115 shares of our common stock will be entitled to rights with respect to the registration of these shares under the Securities Act, as described below. We refer to these shares collectively as registrable securities.

Demand registration rights

Beginning 180 days after the completion of this offering, the holders of at least 62% of the shares of Series B convertible preferred stock then outstanding may make a written request to us for the registration of any of the registrable securities under the Securities Act. We are only required to file two registration statements that are declared effective upon exercise of these demand registration rights. We may postpone the filing of a registration statement once during any 12-month period for a total cumulative period of not more than 90 days if our board of directors determines that the filing would be seriously detrimental to us and our stockholders, provided that we do not register any securities for our own account or any other stockholder during such 90-day period.

Form S-3 registration rights

The holders of at least 20% of the outstanding shares of (i) Preferred Stock (on an as-converted to common stock basis) and (ii) common stock that were issued upon the conversion of shares of Preferred Stock previously held by such Holders can request that we register all or part of their shares on Form S-3 if we are eligible to file a registration statement on Form S-3 and if the aggregate price to the public of the shares offered is at least \$1,000,000. We may postpone the filing of a registration statement on Form S-3 once during any 12-month period for a total cumulative period of not more than 90 days if our board of directors determines that the filing would be seriously detrimental to us and our stockholders, provided that we do not register any securities for our own account or any other stockholder during such 90-day period.

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Piggyback registration rights

In connection with this offering, holders of registrable securities were entitled to, and the necessary percentage of holders waived, their rights to notice of this offering and to include their registrable securities in this offering. If we register any of our securities for public sale in another offering, holders of registrable securities will have the right to include their shares in the registration statement. However, this right does not apply to a registration relating to employee benefit plans or a registration on Form S-4 relating solely to a transaction under Rule 145 of the Securities Act. The underwriters of any underwritten offering will have the right to limit the number of shares registered by these holders if they determine that marketing factors require limitation, in which case the number of shares to be registered will be apportioned pro rata among these holders, according to the total amount of securities entitled to be included by each holder. However, in any underwriting not in connection with an initial public offering, the number of shares to be registered by these holders cannot be reduced below 25% of the total shares covered by the registration statement.

Expenses of registration rights

We generally will pay all expenses related to the registrations, other than underwriting discounts and commissions.

Expiration of registration rights

The registration rights described above will expire, with respect to any particular holder of these rights, on the earlier of the fifth anniversary of the closing of this offering, or when that holder ceases to hold such registrable securities.

Anti-Takeover Provisions

The provisions of Delaware law, and our restated certificate of incorporation and our restated bylaws to be in effect upon the completion of this offering, could have the effect of delaying, deferring or discouraging another person from acquiring control of our company. These provisions, which are summarized below, may have the effect of discouraging takeover bids. They are also designed, in part, to encourage persons seeking to acquire control of us to negotiate first with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with an unfriendly or unsolicited acquirer outweigh the disadvantages of discouraging a proposal to acquire us because negotiation of these proposals could result in an improvement of their terms.

Delaware law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law regulating corporate takeovers. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years following the date on which the person became an interested stockholder unless:

- n Prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- n The interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, but not the outstanding voting stock owned by the interested stockholder, (1) shares owned by persons who are directors and also officers and (2) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or

exchange offer; or

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- n At or subsequent to the date of the transaction, the business combination is approved by the board of directors of the corporation and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66.67% of the outstanding voting stock that is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction or series of transactions together resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation's outstanding voting stock. We expect the existence of this provision to have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. We also anticipate that Section 203 may also discourage attempts that might result in a premium over the market price for the shares of common stock held by stockholders.

Restated Certificate of Incorporation and Restated Bylaw Provisions

Our restated certificate of incorporation and our restated bylaws, to be in effect upon the completion of this offering, include a number of provisions that could deter hostile takeovers or delay or prevent changes in control of our company, including the following:

- n ***Board of Directors vacancies.*** Our restated certificate of incorporation and restated bylaws will authorize our board of directors to fill vacant directorships, including newly created seats unless the board of directors determines that any such vacancies shall be filled by the stockholders. In addition, the number of directors constituting our board of directors is permitted to be set only by a resolution adopted by a majority vote of our entire board of directors. These provisions would prevent a stockholder from increasing the size of our board of directors and then gaining control of our board of directors by filling the resulting vacancies with its own nominees. This makes it more difficult to change the composition of our board of directors but promotes continuity of management.
- n ***Classified board.*** Our restated certificate of incorporation and restated bylaws will provide that our board is classified into three classes of directors, each with staggered three-year terms. A third party may be discouraged from making a tender offer or otherwise attempting to obtain control of us as it is more difficult and time consuming for stockholders to replace a majority of the directors on a classified board of directors. See Management Board Composition.
- n ***Stockholder action; special meetings of stockholders.*** Our restated certificate of incorporation will provide that our stockholders may not take action by written consent, but may only take action at annual or special meetings of our stockholders. As a result, a holder controlling a majority of our capital stock would not be able to amend our restated bylaws or remove directors without holding a meeting of our stockholders called in accordance with our restated bylaws. Further, our restated bylaws will provide that special meetings of our stockholders may be called only by a majority of our board of directors, the chairperson of our board of directors, our Chief Executive Officer or our President, thus prohibiting a stockholder from calling a special meeting. These provisions might delay the ability of our stockholders to force consideration of a proposal or for stockholders controlling a majority of our capital stock to take any action, including the removal of directors.
- n ***Advance notice requirements for stockholder proposals and director nominations.*** Our restated bylaws will provide advance notice procedures for stockholders seeking to bring business before our annual meeting of stockholders or to nominate candidates for election as directors at our annual meeting of stockholders. Our restated bylaws also will specify certain requirements regarding the form and content of a stockholder's notice. These provisions might preclude our stockholders from bringing matters before our annual meeting of

stockholders or from making nominations for directors at our annual meeting of stockholders if the proper

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procedures are not followed. We expect that these provisions might also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

- n ***No cumulative voting.*** The Delaware General Corporation Law provides that stockholders are not entitled to the right to cumulate votes in the election of directors unless a corporation's certificate of incorporation provides otherwise. Our restated certificate of incorporation and restated bylaws will not provide for cumulative voting.
- n ***Directors removed only for cause.*** Our restated certificate of incorporation will provide that stockholders may remove directors only for cause.
- n ***Amendment of charter provisions.*** Any amendment of the above expected provisions in our restated certificate of incorporation would require approval by holders of at least two-thirds of our outstanding common stock, provided that if two-thirds of our board of directors approves such an amendment, then only the approval of a majority of holders is required.
- n ***Issuance of undesignated preferred stock.*** Our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with rights and preferences, including voting rights, designated from time to time by our board of directors. The existence of authorized but unissued shares of preferred stock would enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by merger, tender offer, proxy contest or other means.
- n ***Choice of forum.*** Our restated certificate of incorporation will provide that the Court of Chancery of the State of Delaware will be the exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our restated certificate of incorporation or our restated bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine.

Transfer Agent and Registrar

Upon the completion of this offering, the transfer agent and registrar for our common stock will be American Stock Transfer and Trust Company, LLC. The transfer agent's address is 6201 1st Avenue, Brooklyn, New York 11219, and its telephone number is (800) 937-5449.

Exchange Listing

We have been approved to list our common stock on The NASDAQ Global Market under the symbol AGLE.

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SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock, and we cannot predict the effect, if any, that market sales of shares of our common stock or the availability of shares of our common stock for sale will have on the market price of our common stock prevailing from time to time. Nevertheless, sales of substantial amounts of our common stock, including shares issued upon exercise of outstanding options, in the public market following this offering could adversely affect market prices prevailing from time to time and could impair our ability to raise capital through the sale of our equity securities.

Upon the closing of this offering, we will have a total of 12,929,832 shares of our common stock outstanding, assuming no exercise of the underwriters' option to purchase additional shares, based on the 7,929,832 shares of our capital stock outstanding, on a pro forma basis, as of December 31, 2015. Of these outstanding shares, all of the 5,000,000 shares of common stock sold in this offering will be freely tradable, except that any shares purchased in this offering by our affiliates, as that term is defined in Rule 144 under the Securities Act, could only be sold in compliance with Rule 144.

The remaining outstanding shares of our common stock will be deemed restricted securities as defined in Rule 144. Restricted securities may be sold in the public market only if they are registered under the Securities Act or if they qualify for an exemption from registration under Rule 144 or Rule 701 promulgated under the Securities Act, which rules are summarized below. In addition, substantially all of our security holders have entered into market standoff agreements with us or lock-up agreements with the representatives of the several underwriters under which they have agreed, subject to specific exceptions, not to sell any of our stock for at least 180 days following the date of this prospectus, as described below. As a result of these agreements and the provisions of our amended and restated investors' rights agreement described above under Description of Capital Stock Registration Rights, subject to the provisions of Rule 144 or Rule 701, shares will be available for sale in the public market as follows:

Beginning on the date of this prospectus, all of the shares sold in this offering will be immediately available for sale in the public market; and

Beginning 181 days after the date of this prospectus, 7,929,832 additional shares will become eligible for sale in the public market, of which 4,791,280 shares will be held by affiliates and subject to the volume and other restrictions of Rule 144, as described below, and 87,424 shares will be unvested and subject to our right of repurchase. The amounts above do not reflect any shares purchased pursuant to the directed share program that will be subject to lock-up agreements described under Lock-Up/Market Standoff Agreements below.

Lock-Up/Market Standoff Agreements

All of our directors and officers and substantially all of our security holders are subject to lock-up agreements or market standoff provisions that prohibit them from offering for sale, selling, contracting to sell, granting any option for the sale of, transferring or otherwise disposing of any shares of our common stock, options or warrants to acquire shares of our common stock or any security or instrument related to our common stock, or entering into any swap, hedge or other arrangement that transfers any of the economic consequences of ownership of our common stock, for a period of 180 days following the date of this prospectus without the prior written consent of the representatives of the several underwriters. See Underwriting Lock-Up Agreements.

Participants in the directed share program who purchase more than \$1,000,000 of shares of our common stock shall be subject to a 25 day lock-up with respect to any shares sold to them pursuant to that program. This lock-up will have similar restrictions to the lock-up agreements described in

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Underwriting Lock-Up Agreements. Any shares sold in the directed share program to our directors or executive officers shall be subject to the lock-up agreements described in Underwriting Lock-Up Agreements. See Underwriting Directed Share Program.

Rule 144

In general, under Rule 144 as currently in effect, once we have been subject to public company reporting requirements for at least 90 days, a person who is not deemed to have been one of our affiliates for purposes of the Securities Act at any time during the 90 days preceding a sale and who has beneficially owned the shares proposed to be sold for at least six months, including the holding period of any prior owner other than our affiliates, is entitled to sell those shares without complying with the manner of sale, volume limitation or notice provisions of Rule 144, subject to compliance with the public information requirements of Rule 144. If such a person has beneficially owned the shares proposed to be sold for at least one year, including the holding period of any prior owner other than our affiliates, then that person would be entitled to sell those shares without complying with any of the requirements of Rule 144 described above.

In general, under Rule 144, as currently in effect, our affiliates or persons selling shares on behalf of our affiliates are entitled to sell upon expiration of the lock-up and market standoff agreements described above, within any three-month period, a number of shares that does not exceed the greater of:

- n 1% of the number of shares of our common stock then outstanding, which will equal approximately 129,298 shares immediately after this offering; or
- n the average weekly trading volume of our common stock during the four calendar weeks preceding the filing of a notice on Form 144 with respect to that sale.

Sales under Rule 144 by our affiliates or persons selling shares on behalf of our affiliates are also subject to certain manner of sale provisions and notice requirements and to the availability of current public information about us.

Rule 701

Rule 701 generally allows a stockholder who purchased shares of our common stock pursuant to a written compensatory plan or contract and who is not deemed to have been an affiliate of our company during the immediately preceding 90 days to sell these shares in reliance upon Rule 144, but without being required to comply with the public information, holding period, volume limitation or notice provisions of Rule 144. Rule 701 also permits affiliates of our company to sell their Rule 701 shares under Rule 144 without complying with the holding period requirements of Rule 144. All holders of Rule 701 shares, however, are required by that rule to wait until 90 days after the date of this prospectus before selling those shares pursuant to Rule 701.

Form S-8 Registration Statement

As soon as practicable after the closing of this offering, we intend to file one or more registration statements on Form S-8 under the Securities Act covering all of the shares of our common stock subject to outstanding options and the shares of our common stock reserved for issuance under our stock plans. We expect to file this registration statement as soon as permitted under the Securities Act. However, the shares registered on Form S-8 may be subject to the volume limitations and the manner of sale, notice and public information requirements of Rule 144 and will not be eligible for resale until expiration of the lock-up and market standoff agreements to which they are subject. Of the 629,848 shares of our common stock that were subject to stock options outstanding as of December 31, 2015, options

to purchase 57,066 shares of common stock were vested as of December 31, 2015. Shares of our common stock underlying outstanding options will not be eligible for sale until expiration of the 180 day lock-up and market standoff agreements to which they are subject.

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Registration Rights

We have granted demand, piggyback and Form S-3 registration rights to certain of our stockholders to sell our common stock. Registration of the sale of these shares under the Securities Act would result in these shares becoming freely tradable without restriction under the Securities Act immediately upon the effectiveness of the registration, except for shares purchased by affiliates. For a further description of these rights, see Description of Capital Stock Registration Rights.

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MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS

This section summarizes the material U.S. federal income tax considerations relating to the acquisition, ownership and disposition of our common stock acquired by non-U.S. holders (as defined below) pursuant to this offering. This summary does not provide a complete analysis of all potential U.S. federal income tax considerations relating thereto. The information provided below is based upon provisions of the U.S. Internal Revenue Code of 1986, as amended, or the Code, Treasury regulations promulgated thereunder, administrative rulings and judicial decisions currently in effect. These authorities may change at any time, possibly retroactively, or the Internal Revenue Service, or IRS, might interpret the existing authorities differently. In either case, the tax considerations of owning or disposing of our common stock could differ from those described below. As a result, we cannot assure you that the tax consequences described in this discussion will not be challenged by the IRS or will be sustained by a court if challenged by the IRS.

This summary does not address the tax considerations arising under the laws of any non-U.S., state or local jurisdiction, or under U.S. federal gift and estate tax laws, except to the limited extent provided below. In addition, this discussion does not address tax considerations applicable to an investor's particular circumstances or to investors that may be subject to special tax rules, including, without limitation:

- n banks, insurance companies or other financial institutions;
- n partnerships or entities or arrangements treated as partnerships or other pass-through entities for U.S. federal tax purposes (or investors in such entities);
- n corporations that accumulate earnings to avoid U.S. federal income tax;
- n persons subject to the alternative minimum tax or Medicare contribution tax on net investment income;
- n tax-exempt organizations or tax-qualified retirement plans;
- n controlled foreign corporations or passive foreign investment companies;
- n dealers in securities or currencies;
- n traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;
- n persons that own, or are deemed to own, more than 5% of our capital stock (except to the extent specifically set forth below);
- n certain former citizens or former long-term residents of the United States;
- n persons who hold our common stock as a position in a hedging transaction, straddle, conversion transaction or other risk reduction transaction;
- n persons who do not hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, for investment purposes); or
- n persons deemed to sell our common stock under the constructive sale provisions of the Code.

In addition, if a partnership or entity classified as a partnership for U.S. federal income tax purposes is a beneficial owner of our common stock, the tax treatment of a partner in the partnership or an owner of the entity will depend upon the status of the partner or other owner and the activities of the partnership or other entity. Accordingly, this summary does not address tax considerations applicable to partnerships that hold our common stock, and partners in such partnerships should consult their tax advisors.

INVESTORS CONSIDERING THE PURCHASE OF OUR COMMON STOCK SHOULD CONSULT THEIR OWN TAX ADVISORS REGARDING THE APPLICATION OF THE U.S. FEDERAL INCOME AND ESTATE TAX LAWS TO THEIR PARTICULAR SITUATIONS AND THE CONSEQUENCES OF FOREIGN, STATE OR LOCAL LAWS, AND TAX TREATIES.

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Non-U.S. Holder Defined

For purposes of this summary, a non-U.S. holder is any beneficial owner of our common stock, other than a partnership, that is not:

- n an individual who is a citizen or resident of the United States;
- n a corporation, or other entity taxable as a corporation for U.S. federal income tax purposes, created or organized under the laws of the United States, any state therein or the District of Columbia;
- n a trust if it (i) is subject to the primary supervision of a U.S. court and one of more U.S. persons have authority to control all substantial decisions of the trust or (ii) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person; or
- n an estate whose income is subject to U.S. income tax regardless of source.

If you are a non-U.S. citizen that is an individual, you may, in many cases, be treated as a resident alien, as opposed to a nonresident alien, by virtue of being present in the United States for at least 31 days in the calendar year and for an aggregate of at least 183 days during a three-year period ending in the current calendar year. For these purposes, all the days present in the current year, one-third of the days present in the immediately preceding year, and one-sixth of the days present in the second preceding year are counted. Resident aliens are subject to U.S. federal income tax as if they were U.S. citizens. Such an individual is urged to consult his or her own tax advisor regarding the U.S. federal income tax consequences of the ownership or disposition of our common stock.

Dividends

We do not expect to declare or make any distributions on our common stock in the foreseeable future. If we do make distributions on shares of our common stock, however, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Distributions in excess of our current and accumulated earnings and profits will constitute a return of capital that is applied against and reduces, but not below zero, a non-U.S. holder's adjusted tax basis in shares of our common stock. Any remaining excess will be treated as gain realized on the sale or other disposition of our common stock. See Sale of Common Stock.

Any dividend paid to a non-U.S. holder of our common stock that is not effectively connected with the non-U.S. holder's conduct of a trade or business in the United States will generally be subject to U.S. withholding tax at a 30% rate. The withholding tax might apply at a reduced rate, however, under the terms of an applicable income tax treaty between the United States and the non-U.S. holder's country of residence. You should consult your tax advisors regarding your entitlement to benefits under a relevant income tax treaty. Generally, in order for us or our paying agent to withhold tax at a lower treaty rate, a non-U.S. holder must certify its entitlement to treaty benefits. A non-U.S. holder generally can meet this certification requirement by providing an IRS Form W-8BEN or Form W-8BEN-E (or any successor of such forms) or appropriate substitute form to us or our paying agent. If the non-U.S. holder holds the stock through a financial institution or other agent acting on the holder's behalf, the holder will be required to provide appropriate documentation to the agent. The holder's agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries. If you are eligible for a reduced rate of U.S. federal withholding tax under an income tax treaty, you may obtain a refund or credit of any excess amounts withheld by filing an appropriate claim for a refund with the IRS in a timely manner.

Dividends received by a non-U.S. holder that are effectively connected with a U.S. trade or business conducted by the non-U.S. holder, and if required by an applicable income tax treaty between the United States and the non-U.S.

holder's country of residence, are attributable to a permanent

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establishment maintained by the non-U.S. holder in the United States, are not subject to U.S. withholding tax. To obtain this exemption, a non-U.S. holder must provide us or our paying agent with an IRS Form W-8ECI properly certifying such exemption. Such effectively connected dividends, although not subject to withholding tax, are taxed at the same graduated income tax rates applicable to U.S. persons, net of certain deductions and credits. In addition to being taxed at graduated tax rates, dividends received by corporate non-U.S. holders that are effectively connected with a U.S. trade or business of the corporate non-U.S. holder may also be subject to a branch profits tax at a rate of 30% or such lower rate as may be specified by an applicable tax treaty.

Sale of Common Stock

Subject to the discussions below regarding backup withholding and the Foreign Account Tax Compliance Act, non-U.S. holders will generally not be subject to U.S. federal income tax on any gains realized on the sale, exchange or other disposition of our common stock unless:

- n the gain (i) is effectively connected with the conduct by the non-U.S. holder of a U.S. trade or business and (ii) if required by an applicable income tax treaty between the United States and the non-U.S. holder's country of residence, is attributable to a permanent establishment maintained by the non-U.S. holder in the United States (in which case the special rules described below apply);
- n the non-U.S. holder is an individual who is present in the United States for 183 days or more in the taxable year of the sale, exchange or other disposition of our common stock, and certain other requirements are met (in which case the gain would be subject to a flat 30% tax, or such reduced rate as may be specified by an applicable income tax treaty, which may be offset by certain U.S. source capital losses, even though the individual is not considered a resident of the United States); or
- n the rules of the Foreign Investment in Real Property Tax Act (FIRPTA) treat the gain as effectively connected with a U.S. trade or business.

The FIRPTA rules may apply to a sale, exchange or other disposition of our common stock if we are, or were within the shorter of the five-year period preceding the disposition and the non-U.S. holder's holding period, a U.S. real property holding corporation, or USRPHC. In general, we would be a USRPHC if interests in U.S. real estate comprised at least half of the value of our business assets. We do not believe that we are a USRPHC and we do not anticipate becoming one in the future. Even if we become a USRPHC, as long as our common stock is regularly traded on an established securities market, such common stock will be treated as U.S. real property interests only if beneficially owned by a non-U.S. holder that actually or constructively owned more than 5% of our outstanding common stock at some time within the five-year period preceding the disposition.

If any gain from the sale, exchange or other disposition of our common stock, (i) is effectively connected with a U.S. trade or business conducted by a non-U.S. holder and (ii) if required by an applicable income tax treaty between the United States and the non-U.S. holder's country of residence, is attributable to a permanent establishment maintained by such non-U.S. holder in the United States, then the gain generally will be subject to U.S. federal income tax at the same graduated rates applicable to U.S. persons, net of certain deductions and credits. If the non-U.S. holder is a corporation, under certain circumstances, that portion of its earnings and profits that is effectively connected with its U.S. trade or business, subject to certain adjustments, generally would be subject also to a branch profits tax. The branch profits tax rate is 30% unless reduced by applicable income tax treaty.

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U.S. Federal Estate Tax

The estates of nonresident alien individuals generally are subject to U.S. federal estate tax on property with a U.S. situs. Because we are a U.S. corporation, our common stock will be U.S. situs property and therefore will be included in the taxable estate of a nonresident alien decedent, unless an applicable estate tax treaty between the United States and the decedent's country of residence provides otherwise.

Backup Withholding and Information Reporting

The Code and the Treasury regulations require those who make specified payments to report the payments to the IRS. Among the specified payments are dividends and proceeds paid by brokers to their customers. The required information returns enable the IRS to determine whether the recipient properly included the payments in income. This reporting regime is reinforced by backup withholding rules. These rules require the payors to withhold tax from payments subject to information reporting if the recipient fails to cooperate with the reporting regime by failing to provide his taxpayer identification number to the payor, furnishing an incorrect identification number, or failing to report interest or dividends on his returns. The backup withholding tax rate is currently 28%. The backup withholding rules do not apply to payments to corporations, whether domestic or foreign, provided they establish such exemption.

Payments to non-U.S. holders of dividends on common stock generally will not be subject to backup withholding, and payments of proceeds made to non-U.S. holders by a broker upon a sale of common stock will not be subject to information reporting or backup withholding, in each case so long as the non-U.S. holder certifies its status as a non-U.S. holder (and we or our paying agent do not have actual knowledge or reason to know the holder is a U.S. person or that the conditions of any other exemption are not, in fact, satisfied) or otherwise establishes an exemption. The certification procedures to claim treaty benefits described under "Dividends" will generally satisfy the certification requirements necessary to avoid the backup withholding tax. We must report annually to the IRS any dividends paid to each non-U.S. holder and the tax withheld, if any, with respect to these dividends. Copies of these reports may be made available to tax authorities in the country where the non-U.S. holder resides.

Under the Treasury regulations, the payment of proceeds from the disposition of shares of our common stock by a non-U.S. holder made to or through a U.S. office of a broker generally will be subject to information reporting and backup withholding unless the beneficial owner certifies, under penalties of perjury, among other things, its status as a non-U.S. holder (and the broker does not have actual knowledge or reason to know the holder is a U.S. person) or otherwise establishes an exemption. The payment of proceeds from the disposition of shares of our common stock by a non-U.S. holder made to or through a non-U.S. office of a broker generally will not be subject to backup withholding and information reporting, except as noted below. Information reporting, but not backup withholding, will apply to a payment of proceeds, even if that payment is made outside of the United States, if you sell our common stock through a non-U.S. office of a broker that is:

- n a U.S. person (including a foreign branch or office of such person);
- n a controlled foreign corporation for U.S. federal income tax purposes;
- n a foreign person 50% or more of whose gross income from certain periods is effectively connected with a U.S. trade or business; or
- n a foreign partnership if at any time during its tax year (a) one or more of its partners are U.S. persons who, in the aggregate, hold more than 50% of the income or capital interests of the partnership or (b) the foreign partnership is engaged in a U.S. trade or business;
- n

unless the broker has documentary evidence that the beneficial owner is a non-U.S. holder and certain other conditions are satisfied, or the beneficial owner otherwise establishes an exemption (and the broker has no actual knowledge or reason to know to the contrary).

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Backup withholding is not an additional tax. Any amounts withheld from a payment to a holder of common stock under the backup withholding rules can be credited against any U.S. federal income tax liability of the holder and may entitle the holder to a refund, provided that the required information is furnished to the IRS in a timely manner.

Foreign Account Tax Compliance Act

A U.S. federal withholding tax of 30% may apply to dividends and the gross proceeds of a disposition of our common stock paid to a foreign financial institution (as specifically defined by the applicable rules) unless such institution enters into an agreement with the U.S. government to withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding U.S. account holders of such institution (which includes certain equity holders of such institution, as well as certain account holders that are foreign entities with U.S. owners). This U.S. federal withholding tax of 30% will also apply to dividends and the gross proceeds of a disposition of our common stock paid to a non-financial foreign entity unless such entity provides the withholding agent with either a certification that it does not have any substantial direct or indirect U.S. owners or provides information regarding direct and indirect U.S. owners of the entity. The 30% federal withholding tax described in this paragraph cannot be reduced under an income tax treaty with the United States or by providing an IRS Form W-8BEN or similar documentation. The withholding tax described above will not apply if the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from the rules. Under certain circumstances, a non-U.S. holder might be eligible for refunds or credits of such taxes. Holders should consult with their own tax advisors regarding the possible implications of the withholding described herein.

The withholding provisions described above generally apply to proceeds from a sale or other disposition of common stock if such sale or other disposition occurs on or after January 1, 2019 and to payments of dividends on our common stock.

THE PRECEDING DISCUSSION OF U.S. FEDERAL TAX CONSIDERATIONS IS FOR GENERAL INFORMATION ONLY. IT IS NOT TAX ADVICE. EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE PARTICULAR U.S. FEDERAL, STATE, LOCAL AND FOREIGN TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAWS.

Table of Contents**UNDERWRITING**

We and the representatives of the underwriters for the offering named below will enter into an underwriting agreement with respect to the common stock being offered. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase from us the number of shares of our common stock set forth opposite its name below. UBS Securities LLC, BMO Capital Markets Corp. and Wells Fargo Securities, LLC are the representatives of the several underwriters.

Underwriter	Number of Shares
UBS Securities LLC	2,000,000
BMO Capital Markets Corp.	1,250,000
Wells Fargo Securities, LLC	1,250,000
Needham & Company, LLC	500,000
Total	5,000,000

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent and that the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased, other than those shares covered by the option to purchase additional shares described below. If an underwriter defaults in its obligation to purchase any shares, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against specified liabilities, including liabilities under the Securities Act of 1933, and to contribute to payments the underwriters may be required to make in respect thereof.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel and other conditions specified in the underwriting agreement. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Option to Purchase Additional Shares

We have granted to the underwriters an option to purchase up to 750,000 additional shares of common stock at the public offering price, less the underwriting discount. This option is exercisable for a period of 30 days. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with the sale of the shares of our common stock set forth above. To the extent that the underwriters exercise this option, the underwriters will purchase additional shares from us in approximately the same proportion as shown in the table above.

Discounts and Commissions

The following table shows the public offering price, underwriting discount and proceeds, before expenses, to us. These amounts are shown assuming both no exercise and full exercise of the option to purchase additional shares.

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We estimate that the total expenses of the offering payable by us, excluding underwriting discount, will be approximately \$3.9 million. We have also agreed to reimburse the underwriters for expenses of up to \$45,000 related to the clearance of this offering with the Financial Industry Regulatory Authority, Inc.

	Per Share	Total Without Option	With Option
Public offering price	\$ 10.00	\$ 50,000,000	\$ 57,500,000
Underwriting discount	\$ 0.70	\$ 3,500,000	\$ 4,025,000
Proceeds, before expenses, to us	\$ 9.30	\$ 46,500,000	\$ 53,475,000

The underwriters propose to offer the shares of common stock to the public at the public offering price set forth on the cover of this prospectus. The underwriters may offer the shares of common stock to securities dealers at the public offering price less a concession not in excess of \$0.42 per share. If all of the shares are not sold at the public offering price, the underwriters may change the offering price and other selling terms.

Directed Share Program

At our request, the underwriters have reserved up to 5% of the common stock being offered by this prospectus for sale at the initial public offering price to our directors, officers, employees and other individuals associated with us and members of their families. The sales will be made by UBS Financial Services Inc., a selected dealer affiliated with UBS Securities LLC, an underwriter of this offering, through a directed share program. We do not know if these persons will choose to purchase all or any portion of these reserved shares, but any purchases they do make will reduce the number of shares available to the general public. Any reserved shares not so purchased will be offered by the underwriters to the general public on the same terms as the other shares of common stock. Participants in the directed share program who purchase more than \$1,000,000 of shares shall be subject to a 25 day lock-up with respect to any shares sold to them pursuant to that program. This lockup will have similar restrictions to the lock-up agreements described below. Any shares sold in the directed share program to our directors or executive officers shall be subject to the lock-up agreements described in **Lock-Up Agreements** below.

Discretionary Accounts

The underwriters do not intend to confirm sales of the shares to any accounts over which they have discretionary authority.

Market Information

Prior to this offering, there was no public market for shares of our common stock. The initial public offering price was determined by negotiations between us and the representatives of the underwriters. In addition to prevailing market conditions, the factors considered in these negotiations included:

- n the history of, and prospects for, our company and the industry in which we compete;
- n our past and present financial information;
- n an assessment of our management; its past and present operations, and the prospects for, and timing of, our future revenues;
- n the present state of our development; and

n the above factors in relation to market values and various valuation measures of other companies engaged in activities similar to ours.

An active trading market for the shares may not develop. It is also possible that after the offering the shares will not trade in the public market at or above the initial public offering price.

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We have been approved to list our common stock on The NASDAQ Global Market under the symbol AGLE.

Stabilization

In connection with this offering, the underwriters may engage in stabilizing transactions, over-allotment transactions, syndicate covering transactions, penalty bids and purchases to cover positions created by short sales.

- n Stabilizing transactions permit bids to purchase shares of common stock so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of the common stock while the offering is in progress.
- n Over-allotment transactions involve sales by the underwriters of shares of common stock in excess of the number of shares the underwriters are obligated to purchase. This creates a syndicate short position which may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by the underwriters is not greater than the number of shares that they may purchase in the over-allotment option. In a naked short position, the number of shares involved is greater than the number of shares in the over-allotment option. The underwriters may close out any short position by exercising their option to purchase additional shares and/or purchasing shares in the open market.
- n Syndicate covering transactions involve purchases of common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared with the price at which they may purchase shares through exercise of their option. If the underwriters sell more shares than could be covered by exercise of their option and, therefore, have a naked short position, the position can be closed out only by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that after pricing there could be downward pressure on the price of the shares in the open market that could adversely affect investors who purchase in the offering.
- n Penalty bids permit the representatives to reclaim a selling concession from a syndicate member when the common stock originally sold by that syndicate member is purchased in stabilizing or syndicate covering transactions to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of our common stock. These transactions may be effected on The NASDAQ Global Market, in the over-the-counter market or otherwise and, if commenced, may be discontinued at any time.

Lock-Up Agreements

Pursuant to certain lock-up agreements, we and our executive officers, directors and substantially all of our other stockholders, have agreed, subject to certain exceptions, not to, directly or indirectly, (i) offer, sell, assign, transfer, pledge, contract to sell, or otherwise dispose of any shares of our common stock (including, without limitation, common stock which may be deemed to be beneficially owned by the party to the lock-up agreement in accordance with the rules and regulations promulgated under the Securities Act of 1933, as amended (such shares, beneficially owned shares)) or securities convertible into or exercisable or exchangeable for our common stock, (ii) enter into any

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swap, hedge or similar agreement or arrangement that transfers in whole or in part, the economic risk of ownership of beneficially owned shares or securities convertible into or exercisable or exchangeable for our common stock, whether now owned or hereafter acquired by the party to the lock-up agreement or with respect to which the party to the lock-up agreement has or hereafter acquires the power of disposition, (iii) engage in any short selling of the common stock or securities convertible into or exercisable or exchangeable for our common stock or, (iv) publicly announce the intention to engage in any action described under (i), (ii) or (iii), without the prior written consent of the representatives for a period of 180 days, commencing on, and including, the date of the underwriting agreement and ending on the 180th day following the date of the underwriting agreement.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition. The exceptions permit our executive officers, directors and stockholders, as parties to the lock-up agreements, among other things and subject to restrictions, to: (a) make certain gifts; (b) make transfers by will or intestate succession; (c) if the party is a corporation, partnership, limited liability company or other business entity, make transfers to any stockholders, partners, members of, or owners of similar equity interests in the party, or to an affiliate of the party, if such transfer is not for value; (d) if the party is a corporation, partnership, limited liability company or other business entity, make transfers in connection with the sale or transfer of all of the party's capital stock, partnership interests, membership interests or other similar equity interests, as the case may be, or all or substantially all of the party's assets, in any such case not undertaken for the purpose of avoiding the restrictions imposed by the lock-up agreement; (e) if the party is a trust, make transfers to the settlor or beneficiary of such trust or to the estate of a beneficiary of such trust if such transfer is not for value; (f) enter into transactions relating to shares of common stock acquired by the party in the offering (other than any issuer-directed shares acquired by our directors and officers in this offering) or shares of common stock or other securities convertible into or exchangeable for common stock acquired in open market transactions after completion of the offering, provided that no filing under Section 16(a) of the Exchange Act shall be required or shall be voluntarily made in connection with such transactions; (g) make transfers to us pursuant to agreements under which we have the option to repurchase such common stock or a right of first refusal with respect to transfers of such shares upon termination of service of such party; (h) enter into a 10b5-1 trading plan, provided that such plan does not permit the sale of any common stock during the 180-day lock-up period and no public announcement or filing is made regarding such plan during the 180-day lockup period; (i) make transfers to us to satisfy tax withholding obligations pursuant to our equity incentive plans disclosed in this prospectus; (j) make transfers pursuant to a bona-fide third-party tender offer, merger, consolidation, binding share exchange or other similar transaction made to all holders of our securities involving a change of control of us, provided that in the event such tender offer, merger, consolidation or other transaction is not completed, such securities held by a party will remain subject to the lock-up agreement; (k) transfers of our securities pursuant to a court order or settlement agreement related to the distribution of assets in connection with the dissolution of marriage or civil union; and (l) exercise any option, warrant or other right to acquire our common stock, settlement of any stock-settled appreciation rights, restricted stock or restricted stock units, including through net or cashless exercise, granted and outstanding as of the execution date of the lock-up agreement for such party or upon the completion of the offering; provided that, in the case of clauses (a) through (e), (j) and (k) above, the transferee agrees to be bound in writing by the lock-up restrictions.

The exceptions to the lock-up provision also permit us, among other things and subject to restrictions, to: (a) issue common stock and options to purchase common stock, shares of common stock underlying options granted and other securities, each pursuant to any director or employee stock option plan, stock ownership plan or dividend reinvestment plan we may have in effect on the date of the underwriting agreement and described in this prospectus or the registration statement of which this

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prospectus forms a part; (b) issue common stock pursuant to the conversion of securities or the exercise of warrants, which securities or warrants are outstanding on the date of the underwriting agreement and described in this prospectus or the registration statement of which this prospectus forms a part; (c) adopt a new equity incentive plan, and file a registration statement on Form S-8 under the Securities Act of 1933, as amended, to register the offer and sale of securities to be issued pursuant to such new equity incentive plan, and issue securities pursuant to such new equity incentive plan (including, without limitation, the issuance of shares of common stock upon the exercise of options or other securities issued pursuant to such new equity incentive plan), provided that (1) such new equity incentive plan satisfies the transaction requirements of General Instruction A.1 of Form S-8 under the Securities Act of 1933, as amended, and (2) this clause (c) shall not be available unless each recipient of shares of common stock, or securities exchangeable or exercisable for or convertible into common stock, pursuant to such new equity incentive plan shall be contractually prohibited from selling, offering, disposing of or otherwise transferring any such shares or securities during the remainder of the lock-up period.

Additionally, this lock-up provision does not apply to the conversion of our outstanding preferred shares into common stock in connection with this offering, provided that such common stock received upon conversion will be subject to this lock-up provision.

The representatives may, in their sole discretion and at any time or from time to time before the termination of the lock-up period release all or any portion of the securities subject to lock-up agreements; provided, however, that, subject to limited exceptions, at least three business days before the release or waiver of any lock-up agreement, the representatives must notify us of the impending release or waiver and we will announce the impending release or waiver through a major news service at least two business days before the effective date of the release or waiver.

Electronic Offer, Sale and Distribution of Shares

A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectuses electronically. The representatives may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters and selling group members that will make internet distributions on the same basis as other allocations. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus or the registration statement of which this prospectus forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

Other Relationships

Certain of the underwriters and their affiliates have provided, and may in the future provide, various investment banking, commercial banking and other financial services for us and our affiliates for which they have received, and may in the future receive, customary fees.

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

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instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

United Kingdom

Each of the underwriters has represented and agreed that:

- n it has not made or will not make an offer of the securities to the public in the United Kingdom within the meaning of section 102B of the Financial Services and Markets Act 2000 (as amended) (FSMA) except to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities or otherwise in circumstances which do not require the publication by us of a prospectus pursuant to the Prospectus Rules of the Financial Services Authority (FSA);
- n 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 FSMA) to persons who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 or in circumstances in which section 21 of FSMA does not apply to us; and
- n it has complied with and will comply with all applicable provisions of FSMA with respect to anything done by it in relation to the securities in, from or otherwise involving the United Kingdom.

European Economic Area

In relation to each Member State of the European Economic Area (the "EEA") which has implemented the European Prospectus Directive (each, a "Relevant Member State"), an offer of our shares may not be made to the public in a Relevant Member State other than:

- n to any legal entity which is a qualified investor, as defined in the European Prospectus Directive;
 - n 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 European Prospectus Directive), subject to obtaining the prior consent of the relevant dealer or dealers nominated by us for any such offer, or;
 - n in any other circumstances falling within Article 3(2) of the European Prospectus Directive,
- provided that no such offer of our shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the European Prospectus Directive or supplement prospectus pursuant to Article 16 of the European Prospectus Directive.

For the purposes of this description, the expression an "offer to the public" in relation to the securities 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 the securities to be offered so as to enable an investor to decide to purchase or subscribe for the securities, as the expression may be varied in that Relevant Member State by any measure implementing the European Prospectus Directive in that member state, and the expression "European Prospectus Directive" means Directive 2003/71/EC (and amendments hereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State) and includes any relevant implementing measure in each Relevant Member State. The expression 2010 PD Amending Directive means Directive 2010/73/EU.

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Canada

The securities may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the securities must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Switzerland

The securities will not be offered, directly or indirectly, to the public in Switzerland and this prospectus does not constitute a public offering prospectus as that term is understood pursuant to article 652a or 1156 of the Swiss Federal Code of Obligations.

Israel

In the State of Israel this prospectus shall not be regarded as an offer to the public to purchase shares of common stock under the Israeli Securities Law, 5728 – 1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728 – 1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the "Addressed Investors"); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728 – 1968, subject to certain conditions (the "Qualified Investors"). The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. The company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728 – 1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for our common stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728 – 1968. In particular, we may request, as a condition to be offered common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728 – 1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728 – 1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728 – 1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock; (iv) that the shares of common stock that it will be issued are, subject to exemptions available under

the Israeli Securities Law, 5728 – 1968: (a) for its own account; (b) for investment purposes only; and

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(c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728 – 1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor's name, address and passport number or Israeli identification number.

We have not authorized and do not authorize the making of any offer of securities through any financial intermediary on our behalf, other than offers made by the underwriters and their respective affiliates, with a view to the final placement of the securities as contemplated in this document. Accordingly, no purchaser of the shares, other than the underwriters, is authorized to make any further offer of shares on our behalf or on behalf of the underwriters.

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LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus will be passed upon for us by Fenwick & West LLP, San Francisco, California. The underwriters are being represented by Davis Polk & Wardwell LLP, Menlo Park, California.

EXPERTS

The financial statements as of December 31, 2014 and 2015 and for the years ended December 31, 2014 and 2015 included in this prospectus have been so included in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

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 filed therewith. For further information about us and the common stock offered hereby, reference is made to the registration statement and the exhibits 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 in each instance we refer you to the copy of such contract or other document filed as an exhibit to the registration statement. We currently do not file periodic reports with the SEC. Upon the closing of our initial public offering, we will be required to file periodic reports, proxy statements and other information with the SEC pursuant to the Exchange Act. A copy of the registration statement and the exhibits filed therewith may be inspected without charge at the public reference room maintained by the SEC, located at 100 F Street, NE, Washington, DC 20549, and copies of all or any part of the registration statement may be obtained from that office. 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 of the website is www.sec.gov.

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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Aeglea BioTherapeutics, Inc.:

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations, comprehensive loss, changes in convertible preferred shares/stock and members /stockholders deficit and cash flows present fairly, in all material respects, the financial position of Aeglea BioTherapeutics, Inc. and its subsidiaries at December 31, 2014 and December 31, 2015, and the results of their operations and their cash flows for each of the two years in the period ended December 31, 2015 in conformity with accounting principles generally accepted in the United States of America. 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 of these statements 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. An audit 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.

/s/ PricewaterhouseCoopers LLP

Austin, Texas

March 14, 2016, except with respect to our opinion on the consolidated financial statements insofar as it relates to the reverse stock split described in Note 16 as to which the date is March 28, 2016.

The accompanying notes are an integral part of these consolidated financial statements.

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Table of Contents**Aeglea BioTherapeutics, Inc.****Consolidated Balance Sheets****(In thousands, except share and per share amounts)**

	December 31,		Pro Forma Stockholders Equity December 31, 2015 (unaudited)
	2014	2015	
ASSETS			
CURRENT ASSETS			
Cash and cash equivalents	\$ 2,616	\$ 29,294	
Marketable securities		3,768	
Restricted cash	40	80	
Accounts receivable - grant		1,697	
Deferred offering costs		2,535	
Prepaid expenses and other current assets	74	912	
Total current assets	2,730	38,286	
Property and equipment, net	162	348	
Other non-current assets	38	20	
TOTAL ASSETS	\$ 2,930	\$ 38,654	
LIABILITIES, CONVERTIBLE PREFERRED SHARES AND STOCK, AND MEMBERS AND STOCKHOLDERS DEFICIT			
CURRENT LIABILITIES			
Accounts payable	\$ 345	\$ 176	
Accrued and other current liabilities	713	2,347	
Total current liabilities	1,058	2,523	
Other non-current liabilities		27	
TOTAL LIABILITIES	1,058	2,550	

Commitments (Note 13 and 15)

Series A convertible preferred shares, no par value; 2,361,238 and no shares authorized as of December 31, 2014 and 2015; 2,172,520 and no shares issued and outstanding as of December 31, 2014 and 2015; no shares authorized, issued and outstanding, pro forma (unaudited)

Series A convertible preferred stock, \$0.0001 par value; no shares and 2,172,524 shares authorized as of December 31, 2014 and 2015; no

13,345

13,573

\$

shares and 2,172,520 shares issued and outstanding as of December 31, 2014 and 2015; no shares authorized, issued or outstanding, pro forma (unaudited)

Series B convertible preferred stock, \$0.0001 par value; no shares and 5,008,210 shares authorized as of December 31, 2014 and 2015; no shares and 4,999,976 shares issued and outstanding as of December 31, 2014 and 2015; no shares authorized, issued or outstanding, pro forma (unaudited)

44,738

MEMBERS AND STOCKHOLDERS DEFICIT

Common A-1 shares, no par value; 165,000 and no shares authorized, issued and outstanding as of December 31, 2014 and 2015; no shares authorized, issued or outstanding, pro forma (unaudited)

277

Common A shares, no par value; 2,695,762 and no shares authorized as of December 31, 2014 and 2015; 334,522 and no shares issued and outstanding as of December 31, 2014 and 2015; no shares authorized, issued or outstanding, pro forma (unaudited)

387

Common B shares, no par value; 372,938 and no shares authorized as of December 31, 2014 and 2015; 355,156 and no shares issued and outstanding as of December 31, 2014 and 2015; no shares authorized, issued or outstanding, pro forma (unaudited)

147

Common stock, \$0.0001 par value; no shares and 25,000,000 authorized as of December 31, 2014 and 2015; no shares and 757,336 shares issued and outstanding as of December 31, 2014 and 2015; 7,929,832 issued and outstanding, pro forma (unaudited)

1

Additional paid-in capital

1,373

59,683

Accumulated other comprehensive loss

(1)

(1)

Accumulated deficit

(12,284)

(23,579)

(23,579)

TOTAL MEMBERS AND STOCKHOLDERS DEFICIT

(11,473)

(22,207)

\$

36,104

TOTAL LIABILITIES, CONVERTIBLE PREFERRED SHARES AND STOCK, AND MEMBERS AND STOCKHOLDERS DEFICIT

\$ 2,930

\$ 38,654

The accompanying notes are an integral part of these condensed consolidated financial statements.

Table of Contents**Aeglea BioTherapeutics, Inc.****Consolidated Statements of Operations****(In thousands, except share and per share amounts)**

	Year Ended December 31,	
	2014	2015
Revenues:		
Grant	\$	\$ 6,085
Operating expenses:		
Research and development	\$ 6,830	\$ 11,453
General and administrative	2,074	5,947
Total operating expenses	8,904	17,400
Loss from operations	(8,904)	(11,315)
Other income (expense):		
Interest income	1	22
Change in fair value of forward sale contract	(1,444)	
Other expense, net		(2)
Total other income (expense):	(1,443)	20
Net loss	\$ (10,347)	\$ (11,295)
Deemed dividend to convertible preferred stockholders		(228)
Net loss allocable to common shareholders and stockholders	\$ (10,347)	\$ (11,523)
Class A-1 common:		
Basic and diluted net loss per share	\$ (20.13)	\$
Net loss attributable to class	\$ (3,321)	\$
Basic and diluted weighted-average shares outstanding	165,000	
Class A common:		
Basic and diluted net loss per share	\$ (17.06)	\$
Net loss attributable to class	\$ (5,706)	\$
Basic and diluted weighted-average shares outstanding	334,522	
Class B common:		
Basic and diluted net loss per share	\$ (40.17)	\$
Net loss attributable to class	\$ (1,320)	\$
Basic and diluted weighted-average shares outstanding	32,861	

Common Stock:

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Basic and diluted net loss per share allocable to common stockholders	\$	\$ (19.21)
Net loss allocable to common stockholders	\$	\$ (11,523)
Basic and diluted weighted-average shares outstanding		599,788
Pro forma net loss per share allocable to common stockholders (Note 12, unaudited)		
Basic and diluted net loss per share allocable to common stockholders	\$	\$ (1.69)
Net loss allocable to common stockholders	\$	\$ (11,523)
Basic and diluted weighted-average shares outstanding		6,820,042

The accompanying notes are an integral part of these condensed consolidated financial statements.

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Aeglea BioTherapeutics, Inc.
Consolidated Statements of Comprehensive Loss
(in thousands)

	Year Ended December 31,	
	2014	2015
Net loss	\$ (10,347)	\$ (11,295)
Other comprehensive loss:		
Unrealized loss on marketable securities		(1)
Total comprehensive loss	\$ (10,347)	\$ (11,296)

The accompanying notes are an integral part of these condensed consolidated financial statements.

Table of Contents**Aeglea BioTherapeutics, Inc.****Consolidated Statements of Changes in Convertible Preferred Shares/Stock and Members /Stockholders Deficit****(In thousands)**

Series A Convertible Preferred Shares		Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Common A-1 Shares		Common A Shares		Common B Shares		Common Stock		Additional Paid-in Acc	
Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Capital	Deficit
972	\$ 4,458		\$		\$	165	\$ 277	335	\$ 387		\$		\$	\$	\$
133	845														
1,068	5,575														
	1,936														
	531														
										355	147				
1,173	13,345					165	277	335	387	355	147				
										(1)					
												20			
1,173	(13,345)	2,173	13,345			(165)	(277)	(335)	(387)	(354)	(167)	753		831	

228	(228)
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4,930	43,679
-------	--------

70	1,059
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747

4	23
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\$	2,173	\$ 13,573	5,000	\$ 44,738	\$	\$	\$	757	\$	\$ 1,373	\$
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The accompanying notes are an integral part of these condensed consolidated financial statements.

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Aeglea BioTherapeutics, Inc.
Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,	
	2014	2015
CASH FLOWS FROM OPERATING ACTIVITIES		
Net loss	\$ (10,347)	\$ (11,295)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	19	89
Amortization of premium on marketable securities		2
Loss on disposal of property and equipment		2
Deferred rent		4
Amortization of lease allowance liability		(23)
Share/stock-based compensation	147	767
Change in fair value of forward sale contract	1,444	
Discount on Series A convertible preferred shares	531	
Research and development services settled with convertible preferred stock	845	812
Changes in operating assets and liabilities:		
Accounts receivable-grant		(1,697)
Prepaid expenses and other assets	(112)	(593)
Accounts payable	(165)	(169)
Accrued and other liabilities	303	1,119
Net cash used in operating activities	(7,335)	(10,982)
CASH FLOWS FROM INVESTING ACTIVITIES		
Purchases of property and equipment	(181)	(208)
Purchases of marketable securities		(3,766)
Increase in restricted cash	(40)	(40)
Net cash used in investing activities	(221)	(4,014)
CASH FLOWS FROM FINANCING ACTIVITIES		
Proceeds from issuance of convertible preferred stock, net of issuance costs	5,575	43,679
Proceeds from issuance of common stock		23
Payment of deferred offering costs		(2,028)
Net cash provided by financing activities	5,575	41,674
NET (DECREASE) INCREASE IN CASH	(1,981)	26,678

CASH

Beginning of period	4,597	2,616
End of period	\$ 2,616	\$ 29,294

Supplemental Disclosure of Non-Cash Investing and Financing Information:

Settlement of the forward sale contract for Series A convertible preferred shares	\$ 1,936	\$
Deemed dividend to Series A convertible preferred stockholders upon conversion from an LLC to corporation	\$	\$ 228
Convertible preferred stock issued for research and development services to be performed	\$	\$ 232

The accompanying notes are an integral part of these condensed consolidated financial statements.

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Aeglea BioTherapeutics, Inc.

Notes to Consolidated Financial Statements

1. The Company and Basis of Presentation

Aeglea BioTherapeutics, Inc. (Aeglea or the Company) is a clinical-stage biopharmaceutical company committed to developing enzyme-based therapeutics in the field of amino acid metabolism that it believes will transform the lives of patients with cancer and inborn errors of metabolism, a subset of rare genetic metabolic diseases. The Company operates in one segment and has its principal offices in Austin, Texas.

The Company, founded as Aeglea BioTherapeutics Holdings, LLC (Aeglea LLC), was formed as a Limited Liability Company (LLC) in Delaware on December 16, 2013 and was converted from a Delaware LLC to a Delaware corporation (the LLC Conversion) on March 10, 2015. Except where the context otherwise requires or as otherwise indicated, references to the Company prior to the conversion refer to Aeglea LLC. The LLC Conversion was effective January 1, 2015 for tax purposes and as such, the Company will file a consolidated tax return for the full year ended December 31, 2015.

In connection with the LLC Conversion, all of the equity interests in Aeglea LLC, which consisted of Series A convertible preferred shares, Class A-1 common shares, Class A common shares and Class B common shares, were converted into shares of Series A convertible preferred stock or shares of common stock in the Company. Each Series A convertible preferred share was converted into shares of Series A convertible preferred stock at a ratio of 1.0 to 1.0. Each Class A-1 common share and Class A common share was converted into shares of common stock at a ratio of 1.0 to 1.0. Class B common shares were converted at various ratios depending upon the issuance date of the relevant shares. Vested and unvested Class B common shares of 353,682 were converted into 253,232 shares of vested and unvested restricted common stock and 100,446 vested and unvested options to acquire common stock (see Note 6 and 9).

Since inception, the Company has incurred operating losses and negative cash flow from operations and has no product revenue to date. The Company expects to incur significant expenses, increasing operating losses, and negative cash flows from operations for the foreseeable future. The Company expects its expenses to increase in connection with conducting additional non-clinical studies, conducting clinical trials of its product candidates, seeking regulatory approval for its product candidates and commercializing its product candidates, if approved. The Company may never achieve profitability and, as such, will need to raise additional cash. Accordingly, it will seek to fund its operations through public or private equity or debt financings or other sources, such as research grants. The Company recorded net losses of \$10.3 million and \$11.3 million for the years ended December 31, 2014 and 2015, respectively. The Company had an accumulated deficit of \$12.3 million and \$23.6 million, and net working capital of \$1.7 million and \$35.8 million as of December 31, 2014 and 2015, respectively. The Company has funded its operations primarily through the sale and issuance of convertible preferred shares/stock and common shares/stock and the collection of a research grant. As of December 31, 2014 and 2015, the Company had capital resources consisting of cash, cash equivalents, and marketable securities of \$2.6 million and \$33.1 million, respectively.

The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. In March 2015, the Company issued 4.9 million shares of Series B convertible preferred stock for \$44.0 million in gross proceeds (see Note 6). The Company intends on raising additional capital through the issuance of additional equity and potentially through strategic alliances with partner companies. The Company believes that it has sufficient resources to continue as a going concern for the foreseeable future.

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Aeglea BioTherapeutics, Inc.

Notes to Consolidated Financial Statements

Basis of Presentation

The consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States (U.S. GAAP) as defined by the Financial Accounting Standards Board (FASB) and include the accounts of the Company and its wholly-owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Such management estimates include those related to accruals of research and development related costs, fair values of preferred and common shares and preferred and common stock, a forward sale contract, share-based compensation, and certain company subsidiary income tax related items. Actual results could differ significantly from those estimates.

The Company utilized significant estimates and assumptions in determining the estimated fair value of its Common Stock, Common A-1 shares, Common A shares, and Common B shares, and the forward sale contract for Series A Convertible Preferred Shares. The board of directors determined the estimated fair value of each class of common shares and the common stock based on a number of objective and subjective factors, including external market conditions affecting the biotechnology industry sector, the price at which the Company sold shares of convertible preferred shares, the superior rights and preferences of securities senior to each of the Company's common shares classes, and the marketability at the time. The Company utilized either a hybrid of the Probability-Weighted Expected Return Method (PWERM) and the Option Pricing Method (OPM) or the OPM; both valuation methodologies are based on the Backsolve Method, a form of the market approach, in accordance with the American Institute of Certified Public Accountants, *Audit and Accounting Practice Aid Series: Valuation of Privately Held Company Securities Issued as Compensation*, to estimate the fair value of each class of common shares and common stock. The hybrid valuation methodology applied the PWERM utilizing the probability of going public scenarios and a liquidation scenario. The OPM valuation methodology included estimates and assumptions that require the Company's judgment and considers the respective rights of each class of common shares and common stock. Significant changes to the key assumptions used in the valuations could result in different fair values of Common Stock, Common A-1, Common A, and Common B shares as of the valuation date (See Notes 6, 7, 9, and 10).

Risks and Uncertainties

The product candidates being developed by the Company require approvals from the U.S. Food and Drug Administration (FDA) or foreign regulatory agencies prior to commercial sales. There can be no assurance that the Company's product candidates will receive the necessary approvals. If the Company is denied regulatory approval of its product candidates, or if approval is delayed, it may have a material adverse impact on the Company's business, results of operations and its financial position.

The Company is subject to a number of risks similar to other life science companies, including, but not limited to, risks related to the successful discovery and development of drug candidates, raising additional capital, development of competing drugs and therapies, protection of proprietary technology and market acceptance of the Company's products. As a result of these and other factors and the related uncertainties, there can be no assurance of the Company's future success.

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Aeglea BioTherapeutics, Inc.

Notes to Consolidated Financial Statements

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less at the date of purchase to be cash equivalents. Cash equivalents consist of money market funds and debt securities and are stated at fair value.

Marketable Securities

All investments have been classified as available-for-sale and are carried at estimated fair value as determined based upon quoted market prices or pricing models for similar securities. Management determines the appropriate classification of its investments in debt securities at the time of purchase and reevaluates such designation as of each balance sheet date. Unrealized gains and losses are excluded from earnings and are reported as a component of comprehensive loss. Realized gains and losses and declines in fair value judged to be other than temporary, if any, on available-for-sale securities are included in Other Income (Expense). The cost of securities sold is based on the specific-identification method. There were no realized gains or losses on marketable securities for the years ended December 31, 2014 and 2015. Interest on marketable securities is included in interest income.

Restricted Cash

Restricted cash consists of a money market account held by a financial institution as collateral for the Company's obligations under a corporate credit card agreement. As of December 31, 2014 and 2015, the Company's restricted cash amounted to \$40,000 and \$80,000, respectively.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash, cash equivalents, marketable securities, and restricted cash. The Company's investment policy limits investments to high credit quality securities issued by the U.S. government, U.S. government-sponsored agencies and highly rated banks, subject to certain concentration limits and restrictions on maturities. The Company's cash, cash equivalents, marketable securities, and restricted cash are held by financial institutions in the United States that management believes are of high credit quality. Amounts on deposit may at times exceed federally insured limits. The Company has not experienced any losses on its deposits of cash and cash equivalents and its accounts are monitored by management to mitigate risk. The Company is exposed to credit risk in the event of default by the financial institutions holding its cash and cash equivalents and bond issuers to the extent recorded in the balance sheets.

Deferred Offering Costs

Deferred offering costs, which primarily consist of direct incremental legal, printing, and accounting fees relating to the Company's proposed initial public offering of its common stock (IPO), are capitalized. The deferred offering costs will be offset against IPO proceeds upon the consummation of an offering. In the event the offering is terminated or abandoned, deferred offering costs will be expensed.

Property and Equipment

Property and equipment are stated at cost, net of accumulated depreciation. Depreciation is computed using the straight-line method over the estimated useful lives of the assets. Repairs and maintenance that do not extend the life or improve an asset are expensed as incurred. Upon retirement or sale, the cost of disposed assets and their related accumulated depreciation are removed from the balance sheet. Any gain or loss is credited or charged to operations.

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Table of Contents**Aeglea BioTherapeutics, Inc.****Notes to Consolidated Financial Statements**

The useful lives of the property and equipment are as follows:

Laboratory equipment	5 years
Furniture and office equipment	5 years
Computer equipment	3 years
Software	3 years
Leasehold improvements	Shorter of remaining lease term or estimated useful life

Impairment of Long-Lived Assets

Long-lived assets are reviewed for indications of possible impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparison of the carrying amounts to the future undiscounted cash flows attributable to these assets. An impairment loss is recognized to the extent an asset group is not recoverable, and the carrying amount exceeds the projected discounted future cash flows arising from these assets. There were no impairments of long-lived assets for the years ended December 31, 2014 and 2015.

Accrued Research and Development Costs

The Company records the costs associated with research preclinical studies, clinical trials, and manufacturing development as incurred. These costs are a significant component of the Company's research and development expenses, as a substantial portion of the Company's on-going research and development activities are conducted by third-party service providers, including contract research and manufacturing organizations.

The Company accrues for expenses resulting from obligations under agreements with contract research organizations (CROs), contract manufacturing organizations (CMOs), and other outside service providers for which payment flows do not match the periods over which materials or services are provided to the Company. Accruals are recorded based on estimates of services received and efforts expended pursuant to agreements established with CROs, CMOs, and other outside service providers. These estimates are typically based on contracted amounts applied to the proportion of work performed and determined through analysis with internal personnel and external service providers as to the progress or stage of completion of the services. The Company makes significant judgements and estimates in determining the accrual balance in each reporting period. In the event advance payments are made to a CRO, CMO, or outside service provider, the payments will be recorded as a prepaid asset which will be amortized as the contracted services are performed. As actual costs become known, the Company adjusts its accruals. Inputs, such as the services performed, the number of patients enrolled, or the study duration, may vary from the Company's estimates, resulting in adjustments to research and development expense in future periods. Changes in these estimates that result in material changes to the Company's accruals could materially affect the Company's results of operations. The Company has not experienced any material deviations between accrued and actual research and development expenses.

Leases

The Company entered into a lease agreement for its office facilities. The lease is classified as an operating lease. The Company records rent expense on a straight-line basis over the term of the lease and, accordingly records the difference between cash rent payments and the recognition of rent expense as a deferred rent liability. Incentives granted under the Company's facilities leases, including allowances to fund leasehold improvements, are deferred and are recognized as adjustments to rental expense on a straight-line basis over the term of the lease.

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Aeglea BioTherapeutics, Inc.

Notes to Consolidated Financial Statements

Fair Value of Financial Instruments

The Company uses fair value measurements to record fair value adjustments to certain financial and non-financial assets and liabilities and to determine fair value disclosures. The accounting standards define fair value, establish a framework for measuring fair value, and require disclosures about fair value measurements. Fair value is defined as the price that would be received from selling an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. When determining the fair value measurements for assets and liabilities required to be recorded at fair value, the principal or most advantageous market in which the Company would transact are considered along with assumptions that market participants would use when pricing the asset or liability, such as inherent risk, transfer restrictions, and risk of nonperformance.

The accounting standard for fair value establishes a fair value hierarchy based on three levels of inputs, the first two of which are considered observable and the last unobservable, that requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. A financial instrument's categorization within the fair value hierarchy is based upon the lowest level of input that is significant to the fair value measurement.

The three levels of inputs that may be used to measure fair value are as follows:

- Level 1 Observable inputs, such as quoted prices in active markets for identical assets or liabilities.
- Level 2 Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.
- Level 3 Valuations based on unobservable inputs to the valuation methodology and including data about assumptions market participants would use in pricing the asset or liability based on the best information available under the circumstances.

Financial instruments carried at fair value include cash, cash equivalents, and marketable securities. The carrying amount of accounts receivable, accounts payable and accrued liabilities approximate fair value due to their relatively short maturities.

Convertible Preferred Shares/Stock

The Company records the issuance of all convertible preferred shares/stock net of offering costs on the dates of issuance, which represents the carrying value. The conversion feature of the convertible preferred shares/stock is subject to certain anti-dilution provisions, which if triggered, would require the Company to seek shareholder approval to increase the number of Common A shares/common stock authorized. In the event that the Company cannot deliver the conversion shares because it does not have an adequate number of Common A shares/common stock authorized, the convertible preferred shares/stock would be redeemable. Accordingly, the Company has classified the convertible preferred shares/stock in temporary equity. The Company has not adjusted the carrying value of the convertible preferred shares/stock to their redemption values, since it is uncertain whether or when a redemption event will occur.

Forward Sale Contract for Series A Convertible Preferred Shares

In connection with the issuance of Series A convertible preferred shares on December 24, 2013, the Company entered into a contract for the forward sale of an additional 837,594 Series A convertible preferred shares at a price of \$5.25 per share, contingent upon certain milestones being met. This

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Notes to Consolidated Financial Statements

freestanding financial instrument was classified as a liability because the underlying preferred shares were contingently redeemable. The forward sale contract was carried at fair value on the balance sheet, with changes in fair value recorded in earnings. The liability was settled with the issuance of additional Series A convertible preferred shares on July 15, 2014 (see Note 6).

Revenue Recognition

The Company's sole source of revenue is grant revenue related to a research grant for \$19.8 million received from the Cancer Prevention and Research Institute of Texas (CPRIT), covering a three year period from June 1, 2014 through May 31, 2017. Grant revenue is recognized when qualifying costs are incurred and there is reasonable assurance that the conditions of the award have been met for collection. Proceeds received prior to the costs being incurred are recognized as deferred revenue until the services are performed (see Note 8).

Research and Development Costs

Research and development costs are expensed as incurred. Research and development costs include, but are not limited to, salaries, benefits, travel, share-based compensation, consulting costs, contract research service costs, laboratory supplies, contract manufacturing costs, and costs paid to other third parties that conduct research and development activities on the Company's behalf. Amounts incurred in connection with license agreements are also included in research and development expense.

Certain research and development costs incurred were settled contractually by the Company issuing a variable number of the Company's shares determined by dividing the fixed monetary amount of costs incurred by the issuance-date fair value of the issuable shares. The Company recorded research and development expense for these costs and accrued for the fixed monetary amount as an Accrued Liability as the services were rendered until the amount was settled. In June 2015, the remaining Company obligation to settle these costs with Company shares was converted to a cash-based payment through a contract amendment with the service provider (see Note 13).

Advance payments for goods or services to be rendered in the future for use in research and development activities are deferred and recorded as a prepaid asset. The deferred amounts are expensed as the related goods are delivered or the services are performed.

Share/Stock-Based Compensation

The Company recognizes the cost of share/stock-based awards granted to employees based on the estimated grant-date fair values of the awards. The value of the portion of the award that is ultimately expected to vest is recognized as expense ratably over the requisite service period. The Company recognizes the compensation costs for awards that vest over several years on a straight-line basis over the vesting period (see Note 9). The Company recognizes the cost of share/stock-based awards granted to nonemployees at their then-current fair values as services are performed, and are remeasured through the counterparty performance date.

Income Taxes

Since inception in December 2013 through December 31, 2014, the Company elected to file as a partnership for federal and state income tax purposes. As such, taxable losses from inception through December 31, 2014 were allocated to the members in accordance with the Aeglea LLC operating agreement. Accordingly, income taxes were not provided by the Company, as the losses were included

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Notes to Consolidated Financial Statements

in the members' federal income tax returns. Effective January 1, 2015, the Company, for tax purposes, converted from a partnership to a corporation and will file a corporate income tax return for the full year ended December 31, 2015.

The Company serves as a holding company for seven wholly-owned subsidiary corporations that filed separate income tax returns at the federal and state level for the year ended December 31, 2014. For the year ended December 31, 2015, the Company and its seven wholly-owned subsidiaries will file a consolidated corporate federal income tax return. The Company and its subsidiaries use the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the financial statements and the tax bases of assets and liabilities. A valuation allowance is established against the deferred tax assets to reduce their carrying value to an amount that is more likely than not to be realized. Due to our lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance.

The Company recognizes benefits of uncertain tax positions if it is more likely than not that such positions will be sustained upon examination based solely on the technical merits, as the largest amount of benefits that is more likely than not to be realized upon the ultimate settlement. The Company's policy is to recognize interest and penalties related to the unrecognized tax benefits as a component of income tax expense. To date, there have been no interest or penalties charged in relation to the unrecognized tax benefits.

Comprehensive Loss

Comprehensive loss is the change in members'/stockholders' deficit from transactions and other events and circumstances other than those resulting from investments by members'/stockholders and distributions to members'/stockholders. The Company's other comprehensive loss is currently comprised of changes in unrealized losses on available-for-sale securities.

Unaudited Pro Forma Net Loss per Share Allocable to Common Stockholders

Pro forma basic and diluted net loss per share allocable to common stockholders has been computed to give effect to the automatic conversion of the convertible preferred stockholders' stock into common stock in connection with the Company's initial public offering. The net loss per share allocable to common stockholders does not include the shares expected to be sold and related proceeds to be received from the initial public offering. The convertible preferred stock dividend is included in loss allocable to common stockholders.

Unaudited Pro Forma Stockholders' Equity

Unaudited pro forma equity has been computed to give effect to the automatic conversion of the convertible preferred stock using the if-converted method assuming an IPO had occurred on the most recent reporting date.

Recent Accounting Pronouncements

In August 2014, the FASB issued ASU 2014-15, *Presentation of Financial Statements – Going Concern (Subtopic 205-40): Disclosure of Uncertainties About an Entity’s Ability to Continue as a Going Concern*, which provides guidance on the presentation of management’s plans, when conditions or events raise substantial doubt about the entity’s ability to continue as a going concern within one year after the date that the financial statements are issued. The new standard is effective for fiscal years ending after December 15, 2016. The adoption of this standard is not expected to have a material impact on the Company’s financial statements.

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In April 2015, the FASB issued ASU No. 2015-05, *Intangibles-Goodwill and Other-Internal-Use Software (Subtopic 350-40): Customer's Accounting for Fees Paid in a Cloud Computing Arrangement*, which provides guidance over a customer's accounting for fees paid in a cloud computing arrangement. The guidance is effective for annual periods beginning after December 15, 2015. The adoption will have no impact on the Company's financial statements.

In November 2015, the FASB issued ASU No. 2015-17, *Income Taxes (Topic 740): Balance Sheet Classification of Deferred Taxes*, which requires classification of all deferred tax assets and liabilities as noncurrent on the balance sheet instead of separating deferred taxes into current and noncurrent amounts. In addition, companies will no longer allocate valuation allowances between current and noncurrent deferred tax assets because those allowances will also be classified as noncurrent. This guidance is effective for annual periods beginning after December 15, 2017. Early adoption is permitted. The amendments can be applied either prospectively or retrospectively. The standard will be adopted beginning with the year ended December 31, 2015. Adoption of this guidance did not affect our historical consolidated financial statements.

3. Cash Equivalents and Marketable Securities

The Company held no cash equivalents or marketable securities as of December 31, 2014. The following table summarizes the estimated fair value of our cash equivalents and marketable securities and the gross unrealized gains and losses as of December 31, 2015 (in thousands):

		December 31, 2015		
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Cash equivalents:				
Money market funds	\$ 3,988	\$	\$	\$ 3,988
Reverse repurchase agreements	16,250			16,250
Total cash equivalents	20,238			20,238
Marketable securities:				
US government and agency securities	3,769		(1)	3,768
Total marketable securities	\$ 3,769	\$	\$ (1)	\$ 3,768

All of the investments held as of December 31, 2015 had maturities of less than one year.

As of December 31, 2015, the Company held five debt securities that were in an unrealized loss position for less than one year. The aggregate fair value of debt securities in an unrealized loss position at December 31, 2015 was \$2.5 million with no individual securities in a significant unrealized loss position. The Company evaluated its securities for

other-than-temporary impairment and considered the decline in market value for the securities to be primarily attributable to current economic and market conditions. It is not more likely than not that the Company will be required to sell the securities, and the Company does not intend to do so prior to the recovery of the amortized cost basis. Based on this analysis, these marketable securities were not considered to be other-than-temporarily impaired as of December 31, 2015.

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Property and equipment, net consist of the following (in thousands):

	December 31,	
	2014	2015
Laboratory equipment	\$ 107	\$ 138
Furniture and office equipment		118
Computer equipment	37	79
Software	37	44
Leasehold improvements		77
Property and equipment, gross	181	456
Less: Accumulated depreciation and amortization	(19)	(108)
Property and equipment, net	\$ 162	\$ 348

Depreciation and amortization expense for the years ended December 31, 2014 and 2015 was \$19,000 and \$89,000, respectively. All of the Company's long-lived assets are located in the United States.

5. Accrued and Other Current Liabilities

Accrued and other current liabilities consist of the following (in thousands):

	December 31,	
	2014	2015
Accrued compensation	\$ 269	\$ 571
Accrued contracted research and development costs	277	863
Accrued professional and consulting fees	152	863
Accrued other and other current liabilities	15	50
Total accrued and other current liabilities	\$ 713	\$ 2,347

6. Convertible Preferred Shares/Stock

On December 24, 2013, the Company raised \$5.1 million through the issuance of 971,928 Series A convertible preferred shares at \$5.25 per share. The financing arrangement included a contract for the forward sale of an additional 837,594 Series A convertible preferred shares at a price of \$5.25 per share, contingent upon certain

milestones being met. This freestanding financial instrument was classified as a liability because the underlying preferred shares are contingently redeemable. The fair value of the forward sale contract at issuance was \$440,000. The fair value of the forward sale contract at settlement on July 15, 2014 was \$1.9 million.

The change in fair value of the derivative liability was recorded as Other Income (Expense) in the consolidated statements of operations. For the year ended December 31, 2014, the Company recognized \$1.4 million in expense due to changes in fair value of the derivative liability. The forward sale contract was settled on July 15, 2014 when the Company issued and received payment for additional Series A convertible preferred shares, and the fair value of the financial instrument on that date was reclassified to Series A convertible preferred shares.

On July 15, 2014, the Company raised \$5.6 million through the issuance of 1,067,592 Series A convertible preferred shares at \$5.25 per share (including 837,594 convertible preferred shares related to the forward sale contract). The Series A convertible preferred shares issued on July 15, 2014 were

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recorded at their fair value of \$7.56 per share (see Note 10). The Company recognized \$531,000 in expense for the 229,998 Series A convertible preferred shares that were not covered by the forward sale contract and were issued to an investor providing sponsored research and employees of the company at a discount. The expense was primarily recorded as research and development expense because the counterparties were engaged in such activities on behalf of the Company (see Note 13).

On March 10, 2015, the Company converted from a Delaware limited liability company into a Delaware corporation and changed the Company's name from Aeglea BioTherapeutics Holdings, LLC to Aeglea BioTherapeutics, Inc. In connection with the LLC Conversion, all of the Company's outstanding common shares and convertible preferred shares were converted into shares of common stock and convertible preferred stock. Further, the outstanding Common B share awards were converted into a combination of vested and unvested restricted common stock and vested and unvested stock options with no changes to the vesting provisions (see Note 9). Upon the LLC Conversion, each then-outstanding Series A convertible preferred share was converted into one share of Series A convertible preferred stock, par value \$0.0001 per share. The Company determined that the LLC Conversion resulted in a deemed dividend from stockholders of common stock to stockholders of Series A convertible preferred stock of \$0.11 per share of Series A convertible preferred stock. The Company recorded \$228,000 as an increase in the carrying amount of the Series A convertible preferred stock and as a reduction of additional paid-in capital. Such dividend was determined by comparing the fair value of the Series A convertible preferred shares immediately prior to the conversion to the fair value of the Series A convertible preferred stock issued in the conversion.

Also on March 10, 2015, the Company issued 4,929,948 shares of Series B convertible preferred stock, par value \$0.0001 per share, at an issuance price equal to \$8.93 per share and received gross proceeds of \$44.0 million. In connection with the financing, the Company incurred total issuance costs of \$321,000.

Convertible preferred shares/stock consisted of the following as of December 31, 2014 and 2015 (in thousands, except share amounts):

December 31, 2014					Common A Shares Issuable Upon Conversion
	Preferred Shares Authorized	Preferred Shares Issued and Outstanding	Liquidation Preference	Carrying Value	
Series A convertible preferred shares	2,361,238	2,172,520	\$ 11,406	\$ 13,345	2,172,520

December 31, 2015

	Preferred Stock Authorized	Preferred Stock Issued and Outstanding	Liquidation Preference	Carrying Value	Common Stock Issuable Upon Conversion
Series A convertible preferred stock	2,172,524	2,172,520	\$ 11,406	\$ 13,573	2,172,520
Series B convertible preferred stock	5,008,210	4,999,976	\$ 44,625	\$ 44,738	4,999,976

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The holders of convertible preferred shares/stock have various rights, privileges, and preferences of the convertible preferred shares as follows:

Conversion

Each share of convertible preferred shares/stock is convertible at any time and at the option of the holder into that number of fully-paid and non-assessable common shares/stock determined by dividing the original issue price of the convertible preferred shares/stock by the conversion price in effect on the date of conversion (currently a 1:1 ratio).

Prior to the LLC Conversion and issuance of Series B convertible preferred stock, the Series A convertible preferred shares were automatically convertible into Common A shares at the then-current conversion rate upon (i) a vote of 66% of the outstanding Series A convertible preferred shares, or (ii) the closing of a firm commitment underwritten public offering with (a) aggregate gross proceeds of \$50.0 million (net of underwriters' discounts and commissions) and (b) a per share price for Common A shares equal to or greater than four times the original issue price for the Series A convertible preferred shares.

Subsequent to the LLC Conversion and issuance of Series B convertible preferred stock, each share of convertible preferred stock is automatically converted into shares of common stock at the then-current conversion rate upon (i) a vote of 62% of the outstanding Series B convertible preferred stock, or (ii) the closing of a firm commitment underwritten public offering with (a) aggregate gross proceeds of \$70.0 million (net of underwriters' discounts and commissions) and (b) a per share price for common stock equal to or greater than three times the original issue price for the Series B convertible preferred stock (which implies a per share public offering price of at least \$26.78 per share).

The respective applicable conversion price is subject to adjustment upon any future stock splits or stock combinations, reclassifications or exchanges of similar stock, upon a reorganization, merger or consolidation of the Company, upon the issuance or sale by the Company of common shares/stock for consideration less than the applicable conversion price, or upon the issuance of any share purchase rights that are exercisable at a strike price less than the applicable conversion price.

Dividends

Prior to the LLC Conversion, preferred shares were not entitled to dividends. Subsequent to the LLC Conversion, each share of convertible preferred stock is entitled to non-cumulative dividends of 8% of the original issue price per share, per annum, if, as and when declared by the Board of Directors. Dividends to Series A and Series B stockholders are to be paid in advance of any distributions to common stockholders. No dividends have been declared as of December 31, 2015.

Voting

Each share of convertible preferred shares/stock has voting rights equal to an equivalent number of shares of common shares/stock into which it is convertible and votes together as one class along with the common shares/stock. The

holders of convertible preferred shares/stock have the right to vote on all significant matters as to which holders of common shares/stock have the right to vote.

For as long as at least 342,857 shares of any series of convertible preferred shares/stock (subject to adjustment in the event of a recapitalization affecting the convertible preferred shares/stock) remain outstanding, the Company must obtain the affirmative vote or written consent by at least 66% of the then-outstanding Series A convertible preferred shares prior to the LLC Conversion and 62% of the then-outstanding Series B convertible preferred stock subsequent to the LLC Conversion along with

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Aeglea BioTherapeutics, Inc.

Notes to Consolidated Financial Statements

Board consent to consummate significant transactions including, but not limited to, the authorization and issuance of additional shares or share classes, changing the legal form of the Company from an LLC to a corporation, amending the certificate of incorporation, and the approval of a deemed liquidation event.

Liquidation

In the event of any liquidation, dissolution, or winding up of the Company, either voluntary or involuntary, the holders of the Series A and Series B convertible preferred shares/stock are entitled to be paid out of the assets of the Company an amount per share equal to \$5.25 and \$8.93 respectively, prior to and in preference to any distribution to the holders of common shares/stock.

If assets are insufficient to make payments in full to all holders of Series A and Series B convertible preferred shares/stock, then the assets or consideration will be distributed ratably among the convertible preferred shareholders/stockholders. Prior to the LLC Conversion, distributions were determined based upon the distribution preferences in the LLC agreement discussed further below. Subsequent to the LLC Conversion, remaining assets shall be distributed among the holders of convertible preferred stock and holders of common stock on pro rata basis based on the number of shares held, treating all shares of preferred stock as if they had been converted to common stock pursuant to the then-applicable conversion terms.

LLC Distributions

Prior to the LLC Conversion, the holders of the Series A convertible preferred shares were entitled to receive distributions out of any assets legally available, prior and in preference to any distributions to Common A-1, Common A, and Common B shares, up to the preference amount that equals the original issue price of \$5.25 per share adjusted for share splits, share distributions, combinations and reclassifications.

After the payment of the preference amount to holders of Series A convertible preferred shares, any remaining amount would be paid to the holders of the Series A convertible preferred shares and Common A-1 shares on a pro rata basis; until the Company had distributed an aggregate of \$1 million to the Common A-1 shares. Any remaining amount would be paid to the holders of Series A convertible preferred shares and Common A shares on a pro rata basis; until the Company had distributed to Common A shares an aggregate amount equal to the amount Common A-1 shares received.

Thereafter, if assets remained in the Company, they would be paid to the holders of the Series A convertible preferred shares, Common A-1 shares, Common A shares and Common B shares on a per share pro rata basis; provided that with respect to all Common B shares having a threshold amount, no distribution would be paid with respect to such Common shares until the aggregate amount of all distributions exceed the threshold amount. All Common B Shares were issued with an applicable Threshold Amount set by the Board of Directors to qualify the shares as profits interest within the meaning of Revenue Procedure 93-27 as clarified by Revenue Procedure 2001-43.

To the extent that the amounts available for distribution were insufficient to pay the full amounts to which holders of the shares would otherwise be entitled, the holders of such shares entitled to receive distributions should share ratably

in any such distribution in proportion to the respective amounts that would otherwise be payable.

No distributions were declared or paid by the Company prior to the LLC Conversion.

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The Series A and Series B convertible preferred shares/stock are not mandatorily redeemable as they do not have a set redemption date or date after which the shares/stock may be redeemed by the holders. However, the shares/stock are contingently redeemable upon a deemed liquidation event and the trigger of certain anti-dilution provisions upon conversion to Common A shares/common stock without an adequate number of authorized Common A shares/common stock.

7. Common Shares/Stock

The Company's former LLC Agreement authorized Aeglea LLC to issue three classes of common shares, each with no par value: Common A-1 shares, Common A shares, and Common B shares.

As of December 31, 2014, common shares consisted of the following:

	Shares Authorized	Shares Outstanding
Common A-1	165,000	165,000
Common A	2,695,762	334,522
Common B	372,938	355,156

Aeglea LLC reserved 2,361,238 Common A shares as of December 31, 2014 to allow for conversion of preferred shares to Common A shares. Each share of vested common shares, regardless of class, was entitled to one vote. The holders of each class of common shares were entitled to receive distributions out of any assets legally available, subject to the prior rights and preferences of holders of all classes of shares outstanding (see Note 6).

Common B shares were issued to employees, consultants, and non-employee directors (Note 9). Included in Common B shares outstanding at December 31, 2014 were 261,319 unvested shares issued to employees, consultants, and non-employee directors.

Upon the LLC Conversion, each outstanding Common A-1 and Common A share was automatically converted into one share of common stock, par value \$0.0001 per share. See Note 9 regarding the conversion of outstanding Common B shares. Under the Certificate of Incorporation, the Company authorized 25,000,000 shares of common stock, \$0.0001 par value per share. Each holder of common stock is entitled to one vote for each share of common stock held. The Company's common stock is not entitled to preemptive rights, and is not subject to conversion, redemption or sinking fund provisions. Subject to preferences that may apply to any shares of preferred stock outstanding at the time, the holders of common stock are entitled to receive dividends out of funds legally available if the board of directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that the board of directors may determine.

As of December 31, 2015, the Company had 757,336 shares of common stock issued and outstanding.

8. Grant Revenues

In June 2015, the Company entered into a Cancer Research Grant Contract (Grant Contract) with CPRIT, under which CPRIT awarded a grant not to exceed \$19.8 million for use in developing cancer treatments by exploiting the metabolism of cancer cells. The Grant Contract covers a three year period from June 1, 2014 through May 31, 2017.

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Notes to Consolidated Financial Statements

Upon commercialization of the product, the terms of the Grant Contract require the Company to pay tiered royalties in the low to mid-single digit percentages. Such royalties reduce to less than one percent after a mid-single-digit multiple of the grant funds have been paid to CPRIT in royalties.

The agreement included reimbursement for qualified expenditures incurred and recognized in 2014. Upon execution of the Grant Contract, grant revenue was recognized for the accumulated qualified expenditures paid and recognized in the period from June 1, 2014 through June 30, 2015. For the years ended December 31, 2014 and 2015, the Company recognized \$0 and \$6.1 million in grant revenues for qualified expenditures under the grant. As of December 31, 2014 and 2015, the Company had an outstanding grant receivable of \$0 and \$1.7 million, respectively, for the grant expenditures that were paid but had not been reimbursed.

9. Share/Stock-Based Compensation

2013 Equity Incentive Plan

In 2013, the Company adopted the 2013 Equity Incentive Plan (the 2013 Plan). The 2013 Plan provides incentives to employees, consultants and non-employee directors of the Company by providing incentive awards of Common B shares or any other class of equity authorized by the Company and designated by the Board of Directors as incentive equity. The Company classified the incentive awards as equity-classified grants of unvested stock within the scope of ASC 718.

All Common B Shares were issued with an applicable Threshold Amount set at an amount so as to qualify the Shares as profits interests within the meaning of Revenue Procedure 93-27 as clarified by Revenue Procedure 2001-43. Threshold Amounts were determined by the Board in good faith based on the fair value of the Company as of the grant date. The Threshold Amount of profit interests granted during the year ended December 31, 2014 were between \$12.2 million and \$22.1 million.

The Common B shares were issued upon grant date and held in escrow in the grantee s name, subject to vesting requirements. Unvested shares could participate in any distributions allocated to the Common B shares and would remain in the custody of the Company until vesting occurred, at which time the funds would be released and voting rights commenced.

Under the Company s former LLC agreement, a total of 372,938 shares of Common B shares were reserved for issuance as of December 31, 2014, of which 17,782 were available for future grants. Incentive awards generally vested over a period of four years with one-fourth vesting upon the first anniversary and one-sixteenth vesting quarterly for three years thereafter.

The following table summarizes employee and nonemployee award activity under the 2013 Plan, prior to the LLC Conversion:

	Common B Shares	Weighted Average Grant Date Fair Value	Aggregate Intrinsic Value (in thousands)
Unvested awards as of December 31, 2013		\$	
Granted	355,156	1.66	
Vested	(93,837)	1.56	
Forfeited			
Unvested awards as of December 31, 2014	261,319	\$ 1.70	\$ 776
Vested awards as of December 31, 2014	93,837	1.56	\$ 280

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The Company discusses the valuation of Common B shares and other common shares/stock in Note 10.

Upon the LLC Conversion, the Company terminated the 2013 Plan and adopted the 2015 Equity Incentive Plan (the 2015 Plan). As discussed further below, all Common B shares issued under the 2013 Plan were replaced with stock options and restricted stock issued under the 2015 Plan.

2015 Equity Incentive Plan

The 2015 Plan provides for the Company to sell or issue common stock or restricted common stock, or to grant incentive stock options or nonqualified stock options for the purchase of common stock, to employees, members of the Board of Directors and consultants of the Company. The 2015 Plan is administered by the Board of Directors, or at the discretion of the Board of Directors, by a committee of the Board of Directors. The exercise prices, vesting and other restrictions are determined at the discretion of the Board of Directors, or their committee if so delegated, except that the exercise price per share of stock options may not be less than 100% of the fair market value of the share of common stock on the date of grant, the term of stock options may not be greater than ten years for all grants, and for grantees holding more than 10% of the total combined voting power of all classes of stock, the term may not be greater than five years. Shares of common stock issued upon exercise of stock options are generally issued from new shares of the Company.

The Company generally grants stock-based awards with service conditions only (service-based awards). Awards granted under the 2015 Plan generally vest over four or five years and expire after ten years, although awards have been granted with vesting terms less than four years.

The total number of shares of common stock that may be issued under the 2015 Plan was 1,228,714 shares as of December 31, 2015, of which 594,286 remained available for future grant as of December 31, 2015.

The Company values its common shares and common stock by taking into consideration its most recently available valuation of common shares and common stock performed by management and the Board of Directors as well as additional factors which may have changed since the date of the most recent contemporaneous valuation through the date of grant.

Modification of Common B Share Awards

As discussed in Note 6, in connection with the LLC Conversion on March 10, 2015, the 355,156 Common B share awards outstanding as of December 31, 2014, less subsequent forfeitures of 1,474 shares, were converted into a combination of 253,232 vested and unvested shares of restricted common stock and 100,446 vested and unvested options to purchase common stock (collectively the Replacement Awards) with no changes to the vesting provisions. The modification affected 7 employees.

In accordance with ASC 718, the Company determined the fair value of the Common B share awards held by employees and nonemployees immediately before the Replacement Awards were issued and compared that amount to the then fair value of the Replacement Awards. Given there was no incremental fair value in connection with the

issuance of the Replacement Awards, the Company continues to recognize the compensation expense originally estimated for the Common B shares at the date of grant. The original Common B share values were allocated to stock options and restricted stock awards based on proportionate conversion date fair values.

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Stock options issued during the year ended December 31, 2015 consist of new grants issued subsequent to the LLC Conversion and Replacement Awards from the conversion of the Common B share awards as discussed above. The Company allocated the fair value from the Common B shares to the stock options at the then-applicable conversion date fair value for the Replacement Awards.

The following table summarizes employee and nonemployee stock option activity under the 2015 Plan, subsequent to the LLC Conversion:

	Shares Issuable Under Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of March 10, 2015		\$		\$
Replacement awards	100,446	3.47		
Granted	544,059	4.76		
Exercised	(4,580)	5.04		
Forfeited	(10,077)	5.04		
Outstanding as of December 31, 2015	629,848	\$ 4.55	9.29	\$ 2,833
Options vested and expected to vest as of December 31, 2015	620,320	\$ 4.57	9.29	\$ 2,783
Options exercisable as of December 31, 2015	57,066	\$ 4.76	9.28	\$ 258

During the year ended December 31, 2015, the weighted-average grant date fair value of non-replacement award options granted was \$3.48 and the total intrinsic value of options exercised was \$25,000.

For the year ended December 31, 2015, the Company issued 25,387 stock options to non-employees with 11,279 options vesting in the period.

Restricted Common Stock

As part of the LLC Conversion, the Company has granted restricted common stock with time-based and performance-based vesting conditions. Unvested shares of restricted common stock may not be sold or transferred by the holder. These restrictions lapse according to the time-based vesting conditions of each award.

All restricted stock awards (RSAs) issued during the year ended December 31, 2015 are Replacement Awards from the conversion of the Common B share awards as discussed above. The Company allocated the fair value from the Common B shares to the restricted stock at the then-applicable conversion date fair value.

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Table of Contents**Aeglea BioTherapeutics, Inc.****Notes to Consolidated Financial Statements**

The table below summarizes employee and nonemployee restricted stock activity, subsequent to the LLC Conversion:

	Shares	Weighted Average Grant Date Fair Value
Unvested restricted common stock as of March 10, 2015		\$
Replacement awards	253,232	1.80
Vested	(134,678)	1.76
Forfeited		
Unvested restricted common stock as of December 31, 2015	118,554	\$ 1.85

The fair value of restricted stock awards that vested during the year ended December 31, 2015 was \$933,000.

For the year ended December 31, 2015 (and as part of the LLC Conversion), the Company issued 61,096 RSAs to non-employees with 32,588 RSAs vesting in the period.

Share/Stock-Based Compensation Expense

Total share/stock-based compensation recognized from the 2013 Plan and the 2015 Plan for the years ended December 31, 2014 and 2015 was as follows (in thousands):

	Year Ended December 31,			
	2014		2015	
	Employee	Non-Employee	Employee	Non-Employee
Research and development	\$ 7	\$ 30	\$ 101	\$ 340
General and administrative	107	3	326	
Total share/stock-based compensation expense	\$ 114	\$ 33	\$ 427	\$ 340

The non-employee awards contain both performance and service-based vesting conditions. No expense was recognized for the unvested non-employee shares with only a performance condition nor for the corresponding Replacement Awards for the year ended December 31, 2015. The performance-based vesting conditions represent counterparty performance conditions. The lowest potential aggregate fair values of these awards was \$0 as of and for

the years ended December 31, 2014 and 2015.

As of December 31, 2015, the Company had an aggregate of \$1.6 million and \$171,000 of unrecognized stock-based compensation expense for options and RSAs outstanding, respectively, which is expected to be recognized over a weighted average period of 3.5 years and 2.1 years, respectively.

In determining the fair value of the non-replacement award stock options granted under the 2015 Plan, the Company uses the Black-Scholes option-pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

Expected Term

The Company's expected term represents the period that the Company's stock-based awards are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term). The Company utilizes this method due to lack of historical exercise data and the plain-vanilla nature of the Company's stock-based awards.

Table of Contents**Aeglea BioTherapeutics, Inc.****Notes to Consolidated Financial Statements*****Expected Volatility***

Since the Company is privately held and does not have any trading history for its common stock, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. When selecting comparable publicly traded biopharmaceutical companies on which it has based its expected stock price volatility, the Company selected companies with comparable characteristics to it, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

Risk-Free Interest Rate

The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend

The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

The fair value of the non-replacement award stock options was estimated at the date of grant using a Black-Scholes option-pricing model with the following weighted-average assumptions:

	Year Ended
	December 31, 2015
Expected term	6.29
Expected volatility	87%
Risk-free interest	1.37%
Dividend yield	0%

10. Fair Value Measurements

The Company measures and reports certain financial instruments as assets and liabilities at fair value on a recurring basis. The carrying amount for all financial assets and liabilities held as of December 31, 2014 approximated their fair value. The following table sets forth the fair value of the Company's financial assets and liabilities at fair value on a recurring basis based on the three-tier fair value hierarchy as of December 31, 2015 (in thousands):

		December 31, 2015			
	Level 1	Level 2	Level 3	Total	
Financial Assets					
Money market funds	\$ 3,988	\$	\$	\$ 3,988	
Reverse repurchase agreements		16,250		16,250	
US government and agency securities		3,768		3,768	
Total financial assets	\$ 3,988	\$ 20,018	\$	\$ 24,006	

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The Company measures the fair value of money market funds on quoted prices in active markets for identical asset or liabilities. The Level 2 assets include reverse repurchase agreements and U.S. government and agency securities and are valued based on quoted prices for similar assets in active markets and inputs other than quoted prices that are derived from observable market data.

The Company evaluates transfers between levels at the end of each reporting period. There were no transfers between Level 1 and Level 2 during the periods presented.

The liability for the forward sale contract is considered a Level 3 instrument. The forward sale contract was settled as of December 31, 2014. The following table sets forth a summary of the Company's Level 3 financial instrument as follows (in thousands):

	Forward Liability
Fair value as of December 31, 2013	\$ 492
Change in fair value	1,444
Fair value of financial instruments settled	(1,936)
Fair value as of December 31, 2014	\$

The forward sale contract was settled on July 15, 2014 when the Company issued and received payment for additional Series A convertible preferred shares, and the fair value of the financial instrument of \$1.9 million was reclassified to Series A convertible preferred shares.

Valuation Approach for the Company's Shares and Related Instruments

The Company utilized either a hybrid of the Probability-Weighted Expected Return Method (PWERM) and the Option Pricing Method (OPM) or the OPM, both valuation methodologies are based on the Backsolve Method, a form of the market approach, to estimate the fair value of each class of common shares, preferred shares, and common stock. The hybrid valuation methodology applied the PWERM utilizing the probability of going public scenarios and a liquidation scenario. The OPM valuation methodology included estimates and assumptions that require the Company's judgment. Inputs used to determine estimated fair value of the shares include the equity value of the Company, probabilities of going public by term (from 12.5% to 80% with terms from 0.55 to 0.13 years), risk-adjusted discount rate (30%), discount for lack of marketability (from 30% to 7.5%), expected timing of the liquidity event (from 2.8 to 3.0 years), a risk-free interest rate (from 0.8% to 1.1%) and the expected volatility (70%). Generally, increases or decreases in these unobservable inputs would result in a directionally similar impact to the fair value measurement of the Company's shares.

The fair value of the forward sale contract for Series A convertible preferred shares was measured using a probability-weighted discount approach. Inputs used to determine estimated fair value of the forward sale contract

include the estimated present and future fair values of the Series A convertible preferred shares, the estimated probability of the milestone being achieved (initially 90%), the discount rate (20%), and an estimated time to the milestone event (initially estimated to be ten months). Increases or decreases in the discount rate generally would result in a directionally opposite impact to the fair value measurement of this forward sale contract. Changes in the estimated fair value of the Series A convertible preferred shares generally would result in a directionally similar impact on the fair value measurement of the forward sale contract.

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Table of Contents**Aeglea BioTherapeutics, Inc.****Notes to Consolidated Financial Statements****11. Income Taxes**

For the years ended December 31, 2014 and 2015, the Company recognized no provision or benefit from income taxes. The difference between the Company's provision for income taxes and the amounts computed by applying the statutory federal income tax rate to income before income taxes is as follows (in thousands):

	Year Ended December 31,	
	2014	2015
Tax provision derived by applying the federal statutory rate to income before income taxes	\$ (3,518)	\$ (3,841)
Permanent differences	54	307
Tax credits	(289)	(321)
Losses of LLC entity attributable to the members	730	
Conversion of LLC from partnership to corporation		(21)
Change in the valuation allowance	3,023	3,876
Income tax expense /(benefit)	\$	\$

The components of the deferred tax assets and liabilities consist of the following (in thousands):

	December 31,	
	2014	2015
Deferred tax assets		
Net operating loss carryforward	\$ 3,021	\$ 6,336
Intangible assets	23	41
Accrued expense	91	184
Stock-based compensation		112
Tax credits	303	624
Other		36
Total deferred tax assets	3,438	7,333
Deferred tax liabilities		
Depreciable assets	\$ (30)	\$ (49)
Total deferred tax liabilities	(30)	(49)
Less: Valuation allowance	(3,408)	(7,284)

Deferred tax assets, net	\$	\$
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The Company has established a valuation allowance equal to the net deferred tax asset due to uncertainties regarding the realization of the deferred tax asset based on the Company's lack of earnings history. The valuation allowance increased by approximately \$3.0 million and \$3.9 million during the years ended December 31, 2014 and 2015, respectively, primarily due to continuing loss from operations.

As of December 31, 2014 and 2015, the Company's subsidiaries had U.S. net operating loss carryforwards (NOL) of approximately \$8.9 million and \$18.6 million, respectively, and U.S. tax credit carryforwards of approximately \$303,000 and \$624,000, respectively. The net operating loss and tax credit carryforwards will begin to expire in 2033, if not utilized. The net operating loss carryforwards are subject to Internal Revenue Service adjustments until the statute closes on the year the net operating loss is utilized.

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The Company has not completed a study to assess whether an ownership change has occurred or whether there have been multiple ownership changes since the Company's formation due to the complexity and cost associated with such a study, and the fact that there may be additional such ownership changes in the future. If the Company has experienced an ownership change at any time since its formation, utilization of the NOL or R&D credit carryforwards would be subject to an annual limitation under Section 382 or 383 of the Internal Revenue Code, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term, tax-exempt rate, and then could be subject to additional adjustments, as required. Additionally, the separate return limitation year (SRLY) rules may apply to losses of the Company's seven wholly-owned subsidiary corporations. The SRLY rules limit the consolidated group's use of a subsidiary corporation's net operating losses to the amount of income generated by the subsidiary corporation after it becomes a member of the group. Any limitation may result in expiration of a portion of the NOL or R&D credit carryforwards before utilization. Further, until a study is completed and any limitation known, no amounts are being considered as an uncertain tax position or disclosed as an unrecognized tax benefit. Additionally, the Company does not expect any unrecognized tax benefits to change significantly over the next twelve months. Due to the existence of the valuation allowance, future changes in the Company's unrecognized tax benefits will not impact its effective tax rate. Any carryforwards that will expire prior to utilization as a result of such limitations will be removed from deferred tax assets with a corresponding reduction of the valuation allowance.

The Company files income tax returns in the U.S. and state jurisdictions. The Company is subject to examination by taxing authorities in its significant jurisdictions for the 2013 and subsequent years.

12. Net Loss Per Share Allocable to Common Shareholders/Stockholders

The Company computes net loss allocable per common shareholder and stockholder using the two-class method required for participating securities. The Company considers convertible preferred shares/stock to be participating securities. In the event that the Company paid out distributions, holders of convertible preferred shares/stock would participate in the distribution.

The two-class method is an earnings (loss) allocation method under which earnings (loss) per share is calculated for each class of common share, common stock, and participating security considering a participating security's rights to undistributed earnings (loss) as if all such earnings (loss) had been distributed during the period. The convertible preferred shares/stock do not have an obligation to fund losses and are therefore excluded from the calculation of basic net loss per share. Starting in the first quarter of 2015 in connection with the LLC Conversion, the Company's Series A and B convertible preferred stock are entitled to receive noncumulative dividends and in preference to any dividends on shares of the Company's common stock.

Basic and diluted net loss per share allocable to common shareholders and stockholders is computed by dividing net loss attributable to the applicable class of common share and common stock by the weighted-average number of that class of common share and common stock outstanding during the period. For net loss per share allocable to common stockholders for the year ended December 31, 2015, the effect of the LLC Conversion is presented prospectively from January 1, 2015 as none of the losses for the year ended December 31, 2015 will be allocated to the members of Aeglea LLC. For periods in which the Company generated a net loss, the Company does not include the potential

impact of dilutive securities in diluted net loss per share, as the impact of these items is anti-dilutive. Additionally, the convertible preferred stock dividend is included in the loss allocable to common stockholders.

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The following weighted-average equity instruments were excluded from the calculation of diluted net loss per share because their effect would have been anti-dilutive for the periods presented:

	Year Ended December 31,	
	2014	2015
Series A convertible preferred shares	1,557,870	
Forward sale contract for Series A convertible preferred shares	447,482	
Unvested Class B common shares	151,936	
Series A convertible preferred stock		2,172,520
Series B convertible preferred stock		4,047,734
Unvested restricted common stock		153,355
Options to purchase common stock		450,458

Unaudited Pro Forma Basic and Diluted Net Loss Per Share Allocable to Common Stockholders

The following table sets forth the computation of our unaudited pro forma basic and diluted net loss per share allocable to common stockholders for the year ended December 31, 2015 (in thousands, except share and per share amounts):

Numerator:

Pro forma and historical net loss allocable to common stockholders	\$ (11,523)
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Denominator:

Weighted-average shares outstanding basic and diluted	599,788
Pro forma adjustment to reflect conversion of convertible preferred stock	6,220,254

Weighted-average shares used in computing pro forma net loss per share allocable to common stockholders basic and diluted	6,820,042
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Pro forma net loss per share allocable to common stockholders:

Basic and diluted	\$ (1.69)
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13. Research and License Agreements***Contract Research Agreement***

In December 2013, the Company entered into a contract research agreement with a contract manufacturing organization (CMO) under which the CMO provides research and development services to the Company in exchange for cash and convertible preferred shares.

For the years ended December 31, 2014 and 2015, the Company issued 133,000 Series A convertible preferred shares and 70,028 Series B convertible preferred shares to the CMO, respectively, with fair values of \$845,000 and \$1.1 million, respectively. The number of convertible preferred shares contractually issuable to the counterparty was determined by dividing a fixed monetary amount by the issuance-date fair value of the issued shares. These services are expensed with other Research and Development costs in accordance with the fair value of the consideration paid and as the services are rendered.

The Company was obligated to issue a variable number of shares of convertible preferred stock upon the completion of certain milestones related to the research and development of the Company's products. In June 2015, the contract research agreement was amended to convert the remaining

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Aeglea BioTherapeutics, Inc.

Notes to Consolidated Financial Statements

unmet milestone awards from share-based payments to cash. As of December 31, 2015, all related obligations payable in convertible preferred stock under the agreement have been satisfied.

For the years ended December 31, 2014 and 2015, the Company also paid the CMO cash of \$1.5 million and \$1.8 million, respectively, under the contract research agreement.

University Research Agreement

In December 2013, the Company entered into a research agreement with the University of Texas at Austin (the University). Under the terms of this research agreement, the Company will engage the University to perform certain nonclinical research activities related to the systemic depletion of amino acids for cancer therapy and enzyme replacement for the treatment of patients having inborn metabolic defects.

Under the research agreement, the Company was required to pay the University an annual amount not to exceed \$386,000 during the one year term of the agreement from the effective date. The term under the agreement was extended in 2014 for an additional 2 months with no increase to the maximum expenditure limitation. In 2015, two separate extensions were executed for a combined \$938,000 increase in the maximum expenditure limitation. The effective agreement as of December 31, 2015 expires on August 31, 2016. For the years ended December 31, 2014 and 2015, the Company paid \$386,000 and \$563,000, respectively, to the University under the research agreement.

License Agreements

In December 2013, the Company entered into two license agreements with the University. Under the terms of each license agreement, the University granted the Company an exclusive worldwide license to develop, manufacture, and commercialize therapeutics related to the University's engineered cysteine/cystine degrading enzymes and engineered Methionase degrading enzymes for use in the treatment of human diseases.

Under each license agreement, the Company paid the University an up-front fee of \$10,000 in 2013 and will pay annual license fees increasing from \$5,000 in 2016 to \$25,000 in 2018 and thereafter. The Company may be required to make future payments of up to \$6.4 million contingent upon attainment of various development and regulatory approval milestones for the licensed product in any country. The milestone payments are payable in various amounts upon the start of different phases of clinical trials, application for, and receipt of regulatory approval, with \$5.0 million payable upon the receipt of regulatory approval and a \$500,000 payment payable on final regulatory approval of a second indication. Additionally, upon commercial sales of the product, the Company will be required to pay to the University a single-digit royalty on net sales of the licensed products in any country or region, if such product sales are ever achieved.

14. Related Party Transactions

The spouse of the Company's Chief Executive Officer provides consulting services to the Company. For the years ended December 31, 2014 and 2015, the Company paid \$146,000 and \$433,000, respectively, to the spouse in consulting fees, which were recorded in Research and Development expenses. As of December 31, 2014 and 2015, the

Company had an outstanding liability to the related party of \$47,000, and \$129,000, respectively.

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Table of Contents**Aeglea BioTherapeutics, Inc.****Notes to Consolidated Financial Statements**

One of the founders, a non-employee member of the Company's Board of Directors, entered into a consulting agreement with the Company under which the founder would receive \$50,000 per year for a fixed number of hours of consulting and advisory services and receive 57,142 Common B shares with the vesting contingent on time and performance milestones being achieved. For the years ended December 31, 2014 and 2015, the Company paid \$50,000 and \$50,000, respectively, to the Founder under the consulting agreement. As of December 31, 2014 and 2015, the Company had no outstanding liability to the related party.

15. Commitments and Contingencies

In November 2014, the Company entered into a lease agreement for office space in Austin, TX. The lease commenced in January 2015 and expires three years after the commencement date. In addition the lease provides for a tenant improvement allowance of up to \$69,000. The lease has rent escalation clauses through the lease term. The Company recognizes rent expense on a straight-line basis over the noncancellable term of the lease.

Under the terms of the office lease agreement, the Company provided the lessor with a \$54,000 security deposit. The lessor shall be entitled to retain all or any part of the security deposit for payment in the event of any uncured default by the Company under the terms of the lease. Provided that the Company is not in default under the lease beyond any applicable cure period, the security deposit requirement shall be reduced by \$18,000 each year and returned to the Company.

Future minimum payments, by year and in aggregate, under noncancellable operating leases consist of the following as of December 31, 2015 (in thousands):

2016	\$ 140
2017	144
Thereafter	
	\$ 284

For the years ended December 31, 2014 and 2015, the Company incurred \$17,000 and \$140,000, respectively, in rent expense under noncancellable operating leases.

In August 2015, the Company amended the research agreement with the University of Texas at Austin to further extend the period of performance and increase the limitation of funding to perform additional research. Under the terms of the amendment, the performance period was extended to August 15, 2016 with a remaining \$375,000 expected to be paid in 2016 (see Note 13).

Indemnification

The Company indemnifies each of its officers and directors for certain events or occurrences, subject to certain limits, while the officer or director is or was serving at the Company's request in such capacity, as permitted under Delaware law and in accordance with its certificate of formation, LLC agreement, and subsidiaries' certificates of incorporation and bylaws. The term of the indemnification period lasts as long as an officer or a director may be subject to any proceeding arising out of acts or omissions of such officer or director in such capacity. The maximum amount of potential future indemnification is unlimited; however, the Company currently holds director and officer liability insurance. This insurance allows the transfer of risk associated with the Company's exposure and may

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enable it to recover a portion of any future amounts paid. The Company believes that the fair value of these indemnification obligations is minimal. Accordingly, it has not recognized any liabilities relating to these obligations for any period presented.

16. Subsequent Events

The Company evaluated subsequent events occurring after December 31, 2015 up to March 14, 2016, the date the financial statements were available to be issued. In connection with the reissuance of the consolidated financial statements to reflect the reverse stock split described below, the Company evaluated subsequent events through March 28, 2016.

On March 28, 2016, the Company effected a 10.5-to-1 reverse stock split of all outstanding shares of the Company's capital stock, including its common stock and its convertible preferred stock. All share, option, restricted stock, and per share information presented in the consolidated financial statements has been adjusted to reflect the stock split on a retroactive basis for all periods presented and all share information is rounded down to the nearest whole share after reflecting the reverse stock split. Pursuant to the provisions of the certificate of incorporation effecting the reverse stock split, all of the outstanding convertible preferred stock will automatically convert into common stock in connection with the completion of this offering.

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5,000,000 Shares

Common Stock

PROSPECTUS

UBS Investment Bank

**BMO Capital Markets
Needham & Company**

Wells Fargo Securities

April 6, 2016

Until May 1, 2016, all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This requirement is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.