Aeglea BioTherapeutics, Inc.
Form 424B5
February 05, 2019
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**Filed Pursuant to Rule 424(b)(5)**
**Registration No. 333-217573**

**This preliminary prospectus supplement and the accompanying prospectus relate to an effective registration statement under the Securities Act of 1933, as amended, but the information in this prospectus supplement is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell the securities, and we are not soliciting an offer to buy these securities, in any jurisdiction where the offer or sale is not permitted.**

**Subject to completion, dated February 5, 2019**

**Preliminary prospectus supplement**

**(To prospectus dated May 30, 2017)**

***$50,000,000***

# Aeglea BioTherapeutics, Inc.

## *Common stock*

## *Pre-funded warrants to purchase common stock*

We are offering shares of our common stock and, in lieu of common stock to certain investors that so choose, pre-funded warrants to purchase shares of common stock pursuant to this prospectus supplement and the accompanying prospectus. The purchase price of each pre-funded warrant will equal the price per share at which shares of common stock are being sold to the public in this offering, minus $0.0001, and the exercise price of each pre-funded warrant will equal $0.0001 per share. This prospectus supplement also relates to the offering of the shares of common stock issuable upon exercise of such pre-funded warrants.

Our common stock is quoted on The Nasdaq Global Market under the symbol AGLE. On February 4, 2019, the last reported sales price for our common stock was $9.16 per share. We do not intend to list the pre-funded warrants on The Nasdaq Global Market, any other national securities exchange or any other nationally recognized trading system.

We are an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012 and, as such, we have elected to comply with certain reduced public company reporting requirements.

**An investment in our common stock involves a high degree of risk. Please read Risk factors on page S-7 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement before investing in our securities.**

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

| | Per share | Per pre-funded warrant | Total |
|---|---|---|---|
| Public offering price | $ | $ | $ |
| Underwriting discounts and commissions(1) | $ | $ | $ |
| Proceeds to Aeglea BioTherapeutics, Inc. (before expenses) | $ | $ | $ |

(1) See Underwriting beginning on page S-23 of this prospectus supplement for additional information regarding underwriting compensation.

We have granted the underwriters an option to purchase up to an additional shares of our common stock from us at the public offering price, less the underwriting discounts and commissions, within 30 days from the date of this prospectus supplement.

The underwriters expect to deliver the shares against payment on or about , 2019 through the book entry facilities of the Depository Trust Company. The pre-funded warrants are expected to be delivered on or about , 2019.

*Joint Book-Running Managers*

**J.P. Morgan** **Evercore ISI**

*Lead Manager*

**H.C. Wainwright & Co.**

**Prospectus supplement dated , 2019**

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**Prospectus supplement**

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**Prospectus**

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# About this prospectus supplement

This document is in two parts. The first part is the prospectus supplement, including the documents incorporated by reference herein, which describes the specific terms of this offering and also adds to and updates the information contained in the accompanying prospectus and the documents incorporated by reference therein. The second part, the accompanying prospectus, including the documents incorporated by reference therein, provides more general information, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. Before you invest, you should carefully read this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein, as well as the additional information described in this prospectus supplement under Where you can find more information. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference therein, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference therein. However, if any statement in one of these documents is inconsistent with a statement in another document with a later date that is incorporated by reference herein, the statement in the document having the later date modifies and supersedes the earlier statement.

Neither we nor the underwriters have authorized anyone to provide you with any information or to make any representation, other than those contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, which together we sometimes refer to generally as the prospectus, or in any free writing prospectus prepared by us or on our behalf or to which we have referred you. Neither we nor the underwriters take any responsibility for, and provide no assurance as to the reliability of, any other information that others may give you. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

We are offering to sell, and seeking offers to buy, shares of our common stock and pre-funded warrants only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the offering of the common stock and pre-funded warrants in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement must inform themselves about, and observe any restrictions relating to, the offering of the common stock and pre-funded warrants and the distribution of this prospectus supplement outside the United States. This prospectus supplement does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Unless the context indicates otherwise, as used in this prospectus supplement and the accompanying prospectus, the terms Company, Aeglea, Registrant, we, us and our refer to Aeglea BioTherapeutics, Inc., a Delaware corporation, and its subsidiaries, taken as a whole, unless otherwis noted. Aeglea and all product candidate names are our common law trademarks. This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein contains additional trade names, trademarks and service marks of other companies, which are the property of their respective owners. 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.

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# Prospectus summary

*This summary highlights selected information contained elsewhere in this prospectus supplement and the accompanying prospectus. It does not contain all of the information you should consider before making an investment decision. Before you decide to invest in our common stock, you should carefully read the entire prospectus supplement and the accompanying prospectus and the documents incorporated by reference herein and therein, including the risk factors and the financial statements and related notes included or incorporated by reference herein and therein.*

## Company overview

We are a biotechnology company that designs and develops innovative human enzyme therapeutics for patients with rare genetic diseases and cancer. We believe our novel approach of utilizing human enzymes offers advantages that provide a greater likelihood of clinical success and commercial adoption.

Our drug-hunting capabilities in enzyme engineering, preclinical disease modeling, and drug development in both rare genetic disease and cancer allow us to identify and advance innovative opportunities to address important unmet medical needs for the benefit of patients. Our programs and the decisions we make to progress assets into clinical studies are driven by the following considerations:

- Potential for enhancement of human enzymatic activity
- Ability to create novel human enzymatic activity
- Strong preclinical data and rationale
- Limited or no competition
- Meaningful commercial opportunities
- Worldwide commercial rights

We are a patient-focused organization conscious of the fact that people with a rare genetic disease or cancer have limited treatment options, and we recognize that their lives and well-being are highly dependent upon our efforts to develop improved therapies. For this reason, we are passionate about designing and developing novel therapeutics to address significant unmet medical need for rare genetic disease and cancer.

Our lead product candidate, pegzilarginase, is engineered to degrade the amino acid arginine and is being developed to exploit two aspects of arginine metabolism, including arginine excess in patients with Arginase 1 Deficiency, a rare genetic disease, as well as the arginine dependence of some cancers. We expect to start a single, global pivotal Phase 3 trial of pegzilarginase in patients with Arginase 1 Deficiency in the second quarter of 2019. We are currently evaluating pegzilarginase in multiple ongoing clinical trials, including a Phase 1/2 clinical trial for the treatment of Arginase 1 Deficiency, an open-label extension study for patients with Arginase 1 Deficiency, a Phase 1 clinical trial for the treatment of advanced solid tumors, and a Phase 1/2 combination clinical trial of pegzilarginase with pembrolizumab for the treatment of patients with small cell lung cancer (SCLC). We are also building a pipeline of additional product candidates targeting key amino acids and other metabolites, including AEB4104 for the treatment of homocystinuria, AEB5100 for the treatment of cystinuria, and AEB2109 for the treatment of cancer.

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***Rare genetic diseases***

*Pegzilarginase in patients with Arginase 1 Deficiency*

Arginase 1 Deficiency is a debilitating disease that progresses despite current medical management leading to severe complications and early death. Pegzilarginase is the first ever investigative therapy that addresses the elevated levels of arginine, which is the key driver of Arginase 1 Deficiency.

In December 2018, we announced the design of our single, global pivotal Phase 3 PEACE (Pegzilarginase Effect on Arginase 1 Deficiency Clinical Endpoints) trial with a primary endpoint of plasma arginine reduction and secondary endpoints which include assessments of clinical outcomes on mobility and adaptive behavior, safety and pharmacokinetics. The Phase 3 PEACE trial is designed to assess the effects of treatment with pegzilarginase versus placebo over 24 weeks, and we expect to enroll 30 patients with Arginase 1 Deficiency. We finalized the design of the Phase 3 PEACE trial to be a single, global pivotal trial based on the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) feedback. Patients enrolled in the trial will be randomized on a two-to-one basis to receive weekly infusions of pegzilarginase, or placebo for the double-blind treatment period of 24 weeks. Patients will be considered eligible for the PEACE trial if they exhibit average plasma arginine of greater than 250 μM, are greater than two years of age and have a deficit in mobility or adaptive behavior. All assessments and dose adjustments will be conducted in a blinded fashion at pre-specified intervals. Patients will remain on current disease management for the duration of the Phase 3 PEACE trial. We expect to dose the first patient in the PEACE trial in the second quarter of 2019 and expect that data from the Phase 3 PEACE trial will be available in the first quarter of 2021. The FDA indicated that data from this Phase 3 PEACE trial showing plasma arginine reduction in conjunction with improvements in clinically meaningful aspects of the disease may be sufficient to support a marketing application for pegzilarginase in Arginase 1 Deficiency. Additional interim clinical data from our Phase 1/2 clinical trial reporting repeat dose administration of pegzilarginase is expected in the first half of 2019.

In October 2018, we announced new positive interim clinical data at the 2018 American Society of Human Genetics (ASHG) Conference from our ongoing Phase 1/2 trial of pegzilarginase in patients with Arginase 1 Deficiency. We reported clinical improvements with repeat dose administration of pegzilarginase after only eight weeks, including consistent reduction of arginine and improvement in mobility or adaptive behavior. Pegzilarginase was generally well tolerated; most treatment-related adverse events were mild, and while investigators considered some of the hypersensitivity events as serious adverse events, the hypersensitivity reactions were generally manageable with standard measures and all patients continued study treatment. Additionally, we completed and exceeded our enrollment target with 16 patients in the Phase 1/2 clinical trial.

In addition, we announced in October 2018 that the FDA granted a rare pediatric disease designation to our lead product candidate, pegzilarginase, for the treatment of Arginase 1 Deficiency. This designation by the FDA confirms our eligibility to receive a rare pediatric disease priority review voucher upon approval of a biologics license application for pegzilarginase if completed before October 1, 2022.

*AEB4104 in patients with homocystinuria*

Homocystinuria is an inherited disorder of methionine metabolism caused by mutations in CBS and other genes leading to elevated levels of plasma and tissue homocysteine and homocystine, which affect multiple organ systems and cause early mortality. Current disease management, which includes dietary protein (methionine) restriction, vitamins, and betaine supplementation, is insufficient to effectively control the more severe forms of the disease. Given the severity of the disease, the limitations of current disease management approaches,

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and the data demonstrating improved survival in a preclinical model of the disease, we intend to advance AEB4104 into IND-enabling studies in the first half of 2019. The patent rights to AEB4104 were exclusively licensed to us from the Board of Regents of The University of Texas System, or the University, pursuant to the Amended and Restated License Agreement dated January 31, 2017, as amended, or the Restated License. For more information on the Restated License, see section titled Item 1. Business Licensing in our Annual Report on Form 10-K for the fiscal year ended December 31, 2017.

In October 2018, we announced preclinical efficacy data on our AEB4104 homocystinuria program at the 2018 American Society of Human Genetics (ASHG) Conference, demonstrating that AEB4104 improved survival and important disease-related abnormalities in a preclinical model of homocystinuria. AEB4104 decreased homocysteine and homocystine levels in the plasma, including the CBS deficient model (CBS-/-) and the high methionine diet-induced model of homocystinuria. Treatment with AEB4104 prevented early mortality, stopped disease progression, and reversed liver pathology.

*AEB5100 in patients with cystinuria*

AEB5100 is a novel recombinant human enzyme that degrades plasma cystine and cysteine. We are developing AEB5100 for the treatment of patients with cystinuria, a rare genetic disease characterized by frequent and recurrent kidney stone formation requiring multiple procedural interventions and by an increased risk of chronic kidney disease. Cystinuria occurs due to genetic mutations in amino acid transporters that lead to increased amounts of cystine in the urine. This results in high cystine concentrations in the urine and formation of kidney stones.

In October 2018, we announced preclinical efficacy data on our AEB5100 cystinuria therapeutic program at the 2018 American Society of Nephrology (ASN) Conference, demonstrating that AEB5100 lowered blood levels of cystine and cysteine, decreased the amount of cystine in the urine and reduced kidney stone formation in a preclinical model of cystinuria. Given the compelling preclinical data and the limitations of current disease management approaches, we intend to advance AEB5100 into IND-enabling studies and we anticipate beginning GLP manufacturing for toxicology studies in the first half of 2019. The patent rights to AEB5100 were exclusively licensed to us from the University pursuant to the Restated License. For more information on the Restated License, see section titled Item 1. Business Licensing in our Annual Report on Form 10-K for the fiscal year ended December 31, 2017.

***Cancer***

*Pegzilarginase with pembrolizumab in patients with small cell lung cancer*

In the first quarter of 2018, we initiated a Phase 1 clinical collaboration with Merck to evaluate the combination of pegzilarginase with Merck s anti-PD1 therapy, pembrolizumab, for the treatment of patients with SCLC, with the primary objectives of determining the safety and dose of pegzilarginase that can be combined with pembrolizumab to be used in Phase 2. The Phase 2 primary objective is objective response rate (ORR) and secondary objectives include safety, clinical benefit rate, time to response, duration of response, progression free survival (PFS), overall survival, pegzilarginase pharmacokinetics, and exploring the correlation of tumor expression of ASS1 and PD-L1 with clinical activity. We dosed the first patient in the first quarter of 2018, expect to initiate Phase 2 in the second quarter of 2019, and expect to report topline safety and clinical activity for Phase 1 in the first quarter of 2019.

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*Pegzilarginase in patients with advanced solid tumors*

In October 2018, we presented interim clinical data at the European Society for Medical Oncology (ESMO) 2018 Congress, demonstrating that pegzilarginase monotherapy resulted in anti-tumor activity in heavily pre-treated patients with advanced melanoma. The investigator-assessed responses in 13 cutaneous melanoma patients and 15 uveal melanoma patients revealed that one patient achieved a confirmed partial response (PR) at week 20 and eight patients had stable disease (SD) at week 8 or later. Three patients experienced treatment-related, serious Grade 3 adverse events, including asthenia and failure to thrive, vomiting and dehydration. Six patients remained on treatment at the time of the data cutoff. Anti-tumor activity appeared greater in tumors lacking argininosuccinate synthetase 1 (ASS1) expression, which is consistent with preclinical studies that suggest tumors lacking ASS1 expression are dependent on extracellular arginine for survival.

In addition, pegzilarginase was shown to rapidly and sustainably deplete plasma arginine with a manageable safety profile. The results, combined with preclinical evidence of synergy with immune checkpoint inhibitors, support further clinical evaluation of pegzilarginase in immunotherapy combinations.

## Recent financial information

We have not finalized our financial statements for the year ended December 31, 2018. Based on our current estimates, as of December 31, 2018, we had approximately $74.5 million in cash and cash equivalents and marketable securities. The actual amounts that we report will be subject to our financial closing procedures and any final adjustments that may be made prior to the time our financial results for the year ended December 31, 2018, are finalized and filed with the Securities and Exchange Commission. The preliminary financial data included herein has been prepared by, and is the responsibility of, our management. PricewaterhouseCoopers LLP has not audited, reviewed, compiled, or applied agreed-upon procedures with respect to the preliminary financial data. Accordingly, PricewaterhouseCoopers LLP does not express an opinion or any other form of assurance with respect thereto.

## 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. 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 supplement, and you should not consider information on our website to be part of this prospectus supplement.

## JOBS Act

We are an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We will remain an emerging growth company until the earlier of the last day of the fiscal year following the fifth anniversary of the completion of our initial public offering in April 2016, the last day of the fiscal year in which we have total annual gross revenue of at least $1.07 billion, the date on which we are deemed to be a large accelerated filer (this means that at the end of a fiscal year we have been public for at least 12 months, have filed at least one annual report and the market value of our common stock that is held by non-affiliates exceeds $700 million as of the end of the second quarter of that fiscal year), or the date on which we have issued more than $1.0 billion in nonconvertible debt securities during the prior three-year period.

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# The offering

| | |
|---|---|
| **Common stock offered by us** | shares |
| **Pre-funded warrants offered by us** | We are also offering, in lieu of common stock to certain purchasers, pre-funded warrants to purchase shares of common stock. The purchase price of each pre-funded warrant will equal the price per share at which the shares of common stock are being sold to the public in this offering, minus $0.0001, and the exercise price of each pre-funded warrant will be $0.0001 per share. Each pre-funded warrant will be exercisable from the date of issuance until the fifth anniversary of the date of issuance, subject to an ownership limitation. See Description of pre-funded warrants. This prospectus supplement also relates to the offering of the shares of common stock issuable upon exercise of such pre-funded warrants. |
| **Common stock to be outstanding after this offering** | shares |
| **Option to purchase additional shares** | We have granted the underwriters an option for a period of 30 days to purchase an additional shares of common stock. The number of shares subject to the underwriters option will equal 15% of the total number of shares of common stock we are offering plus the shares underlying the pre-funded warrants. |
| **Use of proceeds** | We estimate that the net proceeds of this offering, after deducting underwriting discounts and commissions and estimated offering expenses, will be approximately $46.7 million, or $53.7 million if the underwriters option is exercised in full. We intend to use the net proceeds of this offering, together with our existing cash resources, to advance the clinical development of pegzilarginase through our Phase 3 pivotal and extension trials in Arginase 1 Deficiency and an ongoing combination trial in cancer, and the remainder to fund continued IND-enabling activities of multiple of our pipeline programs, research and development, manufacturing, initial commercialization infrastructure and for working capital and general corporate purposes. See Use of proceeds. |
| **Risk factors** | Investing in our common stock involves significant risks. See Risk factors, beginning on page S-7 as well as the other information included in or incorporated by reference in this prospectus supplement and the accompanying prospectus, for a discussion of risks you should carefully consider before investing in our securities. |
| **Nasdaq Global Market symbol** | AGLE |

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The number of shares of our common stock to be outstanding immediately after this offering as shown above is based on 22,098,218 shares of common stock outstanding as of September 30, 2018 and excludes the shares of common stock issuable upon exercise of the pre-funded warrants being offered by us in this offering, as well as:

- 3,031,347 shares of common stock issuable upon exercise of options outstanding as of September 30, 2018, with a weighted average exercise price of $6.16 per share;
- 418,900 shares of common stock issuable upon exercise of options granted after September 30, 2018, with a weighted average exercise price of $9.23 per share;
- 1,121,472 shares of common stock reserved and available for future issuance as of September 30, 2018, under our equity incentive plans, consisting of (1) 84,521 shares of common stock reserved and available for issuance under our 2016 Equity Incentive Plan as of September 30, 2018, (2) 50,851 shares of common stock reserved for issuance under our 2016 Employee Stock Purchase Plan as of September 30, 2018, (3) 986,100 shares of common stock reserved for issuance under our 2018 Equity Inducement Plan as of September 30, 2018;
- 1,759,602 additional shares of common stock reserved and available for future issuance under our 2016 Equity Incentive Plan as of October 8, 2018;
- 1,845,820 shares of common stock sold under our at-the-market program with JonesTrading Institutional Services LLC in October 2018, which we terminated in December 2018; and
- shares of our common stock that may be sold from time to time under an at-the-market program that we entered into in December 2018 with Jefferies LLC.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise of outstanding options and, no exercise of the underwriters option to purchase additional shares of common stock and no exercise of the pre-funded warrants we are offering to certain purchasers.

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# Risk factors

*An investment in our securities involves a high degree of risk. Prior to making a decision about investing in our securities, you should carefully consider the risk factors described below together with all of the risks, uncertainties and assumptions discussed under Part II, Item 1A, Risk Factors, in our Quarterly Report on Form 10-Q for the period ended September 30, 2018, which is incorporated herein by reference, and may be amended, supplemented or superseded from time to time by other reports we file with the Securities and Exchange Commission, or SEC, in the future. If any of the risks incorporated by reference or set forth below occurs, our business, operations and financial condition could suffer significantly. As a result, you could lose some or all of your investment in our common stock and pre-funded warrants. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business, operations and financial condition, or cause the value of our common stock to decline.*

## Risks related to this offering

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

Our management has broad discretion in the application of the net proceeds from this offering, 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.

***If you purchase shares of common stock sold in this offering you will experience immediate and substantial dilution in your investment. You will experience further dilution if we issue additional equity securities in the future.***

Since the price per share of our common stock being offered is higher than the net tangible book value per share of our common stock, you will suffer dilution with respect to the net tangible book value of the shares of common stock you purchase in this offering. Based on a public offering price of $ per share and our net tangible book value as of September 30, 2018, if you purchase shares of common stock in this offering, you will suffer immediate dilution of $ per share with respect to the net tangible book value of the common stock. Furthermore, if outstanding options or the pre-funded warrants offered hereby are exercised, you could experience further dilution. See Dilution for a more detailed discussion of the dilution you will incur if you purchase shares of common stock in this offering.

***Future sales of our common stock in the public market 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 and make it more difficult for you to sell your common stock at a time and price that you deem appropriate.

We may raise money through additional public or private offerings of our equity securities or equity-linked securities. For example, in December 2018, we entered into an at-the-market program with Jefferies LLC

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pursuant to which we may sell shares of our common stock from time to time, subject to certain conditions. Any sales of our equity or equity-linked securities could have a material adverse effect on the market price of our common stock.

In connection with this offering, we and our directors and executive officers have entered into lock-up agreements for a period of 90 days following this offering. The lock-up agreements are subject to various exceptions, and we and our directors and executive officers may be released from the lock-up agreements prior to the expiration of the lock-up period at the sole discretion of the representatives. See Underwriting. Upon expiration or earlier release of the lock-up agreements, we and our directors and executive officers may sell shares into the market, which could adversely affect the market price of shares of our common stock.

Certain holders of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements under the Securities Act of 1933, as amended, or the Securities Act, that we may file for ourselves or other stockholders. Once we register these shares, they can be freely sold in the public market. Moreover, we have also registered under the Securities Act shares of common stock that we may issue under our equity compensation and inducement plans.

In addition, we have a significant number of stock options outstanding, and may also choose to issue additional common stock, or securities convertible into or exchangeable for common stock, in the future in connection with a financing, an acquisition, a litigation settlement, employee arrangements or otherwise. In the event that the outstanding options are exercised, or that we make additional issuances of common stock or other convertible or exchangeable securities, you could experience additional dilution. Furthermore, we cannot assure you that we will be able to issue shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering, and investors purchasing our securities in the future may have rights superior to investors purchasing shares in this offering.

***There is no public market for the pre-funded warrants being offered in this offering.***

There is no public trading market for the pre-funded warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply to list the pre-funded warrants on any securities exchange or nationally recognized trading system, including the Nasdaq Global Market. Without an active market, the liquidity of the pre-funded warrants will be limited.

***We will not receive any additional funds upon the exercise of the pre-funded warrants.***

Each pre-funded warrant will be exercisable at any time on or after the date of issuance until the fifth anniversary of its issuance and only by way of a cashless exercise, meaning that the holder would not pay a cash purchase price upon exercise, but instead would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the pre-funded warrant. Accordingly, we will not receive any additional funds upon the exercise of the pre-funded warrants.

***Holders of pre-funded warrants purchased in this offering will have no rights as common stockholders until such holders exercise their pre-funded warrants and acquire our common stock.***

Until holders of pre-funded warrants acquire shares of our common stock upon exercise of the pre-funded warrants, holders of pre-funded warrants will have no rights with respect to the shares of our common stock underlying such pre-funded warrants. Upon exercise of the pre-funded warrants, the holders will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

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***Significant holders or beneficial holders of our common stock may not be permitted to exercise pre-funded warrants that they hold.***

A holder of a pre-funded warrant will not be entitled to exercise any portion of any pre-funded warrant which, upon giving effect to such exercise, would cause (i) the aggregate number of shares of our common stock beneficially owned by the holder (together with its affiliates) to exceed 4.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise, or (ii) the combined voting power of our securities beneficially owned by the holder (together with its affiliates) to exceed 4.99% of the combined voting power of all of our securities then outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. As a result, you may not be able to exercise your pre-funded warrants for shares of our common stock at a time when it would be financially beneficial for you to do so, or prior to the expiration of the pre-funded warrants. In such circumstance you could seek to sell your pre-funded warrants to realize value, but you may be unable to do so in the absence of an established trading market for the pre-funded warrants.

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# Forward-looking statements

This prospectus supplement, the accompanying prospectus, and documents incorporated by reference herein and therein contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements involve a number of risks and uncertainties. We caution readers that any forward-looking statement is not a guarantee of future performance and that actual results could differ materially from those contained in the forward-looking statement. These statements are based on current expectations of future events. Such statements include, but are not limited to, statements about future financial and operating results, plans, objectives, expectations and intentions, costs and expenses, outcome of contingencies, financial condition, results of operations, liquidity, cost savings, objectives of management, business strategies, financing, the timing, plans and expected results of our current and future preclinical studies and clinical trials, the length of time that we believe our existing cash resources will fund operations, the extent to which we will be able to advance development of our product candidates using the proceeds of this offering together with our existing cash resources; clinical and commercial collaboration with third-parties, the receipt and timing of potential regulatory designations, our ability to maintain and recognize the benefits of certain designations received by product candidates, the achievement of clinical and commercial milestones, the advancement of our technologies and our proprietary product candidates, approvals and commercialization of product candidates and other statements that are not historical facts. You can find many of these statements by looking for words like believes, expects, anticipates, estimates, may, might, should, will, cou intend, project, seek or similar expressions in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein and any free writing prospectus. We intend that such forward-looking statements be subject to the safe harbors created thereby.

These forward-looking statements are based on the current beliefs and expectations of our management and are subject to significant risks and uncertainties. If underlying assumptions prove inaccurate or unknown risks or uncertainties materialize, actual results may differ materially from current expectations and projections. Factors that might cause such a difference include those discussed in Part II, Item 1A Risk Factors in our Quarterly Report on Form 10-Q for the period ended September 30, 2018, as well as those discussed in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein and any free writing prospectus. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date made.

All subsequent written or oral forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section. We do not undertake any obligation to release publicly any revisions to these forward-looking statements to reflect events or circumstances after the date of this prospectus supplement or to reflect the occurrence of unanticipated events, except as may be required under applicable U.S. securities laws. If we do update one or more forward-looking statements, no inference should be drawn that we will make additional updates with respect to those or other forward-looking statements.

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# Use of proceeds

We estimate that the net proceeds of this offering, after deducting underwriting discounts and commissions and estimated offering expenses, will be approximately $46.7 million, or $53.7 million if the underwriters option to purchase additional shares is exercised in full. We will not receive any additional proceeds from the exercise of the pre-funded warrants.

We intend to use the net proceeds of this offering, together with our existing cash resources, to advance the clinical development of pegzilarginase through our Phase 3 pivotal and extension trials in Arginase 1 Deficiency and an ongoing combination trial in cancer, and the remainder to fund continued IND-enabling activities of multiple of our pipeline programs, research and development, manufacturing, initial commercialization infrastructure and for working capital and general corporate purposes.

The amounts and timing of our actual expenditures will depend on numerous factors, including the progress of our clinical trials and other development efforts and other factors described under Risk factors in this prospectus supplement and the documents incorporated by reference herein, as well as the amount of cash used in our operations. As a result, our management will have broad discretion over the uses of the net proceeds, if any, we receive in connection with securities offered pursuant to this prospectus supplement and investors will be relying on the judgment of our management regarding the application of the proceeds. Pending these uses, we intend 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 capital stock. We currently intend to retain any future earnings for use in the operation of our business and do not intend to declare or pay any cash dividends in the foreseeable future. Any further determination to pay dividends on our capital stock will be at the discretion of our board of directors, subject to applicable laws, and will depend on our financial condition, results of operations, capital requirements, general business conditions and other factors that our board of directors considers relevant.

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# Dilution

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

Our net tangible book value as of September 30, 2018 was approximately $63.7 million, or $2.88 per share. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of September 30, 2018. Dilution with respect to net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering.

After giving effect to the sale of shares of our common stock and pre-funded warrants to purchase up to shares of our common stock at the public offering price of $ per share of common stock and $ per pre-funded warrant (which equals the public offering price per share of the common stock less the $0.0001 per share exercise price of each such pre-funded warrant) (and excluding shares of common stock issued and any proceeds received upon exercise of the warrants or any resulting accounting associated with the warrants) and after deducting underwriting discounts and commissions and estimated offering expenses, our as adjusted net tangible book value as of September 30, 2018 would have been approximately $ million, or $ per share. This represents an immediate increase in net tangible book value of $ per share to existing stockholders and immediate dilution of $ per share to investors purchasing our common stock and pre-funded warrants in this offering at the public offering price. The following table illustrates this dilution on a per share basis:

| | | |
|---|---|---|
| Public offering price per share | | $ |
| Net tangible book value per share as of September 30, 2018 | $ 2.88 | |
| Increase in net tangible book value per share attributable to investors purchasing our common stock and pre-funded warrants in this offering | | |
| As adjusted net tangible book value per share after this offering | | |
| Dilution per share to investors purchasing our common stock in this offering | | $ |

If holders of pre-funded warrants exercise the pre-funded warrants, the as adjusted net tangible book value per share of our common stock after giving effect to this offering would be $ per share, and the dilution in net tangible book value per share to investors purchasing common stock in this offering would be $ per share. If the underwriters exercise their option to purchase additional shares in full, the as adjusted net tangible book value per share of our common stock after giving effect to this offering would be $ per share, and the dilution in net tangible book value per share to investors purchasing common stock in this offering would be $ per share.

The number of shares of our common stock to be outstanding immediately after this offering as shown above is based on 22,098,218 shares of common stock outstanding as of September 30, 2018 and excludes the shares of common stock issuable upon the exercise of the pre-funded warrants being offered by us in this offering, as well as:

- 3,031,347 shares of common stock issuable upon exercise of options outstanding as of September 30, 2018, with a weighted average exercise price of $6.16 per share;

- 418,900 shares of common stock issuable upon exercise of options granted after September 30, 2018, with a weighted average exercise price of $9.23 per share;

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- 1,121,472 shares of common stock reserved and available for future issuance as of September 30, 2018, under our equity incentive plans, consisting of (1) 84,521 shares of common stock reserved and available for issuance under our 2016 Equity Incentive Plan as of September 30, 2018, (2) 50,851 shares of common stock reserved for issuance under our 2016 Employee Stock Purchase Plan as of September 30, 2018, (3) 986,100 shares of common stock reserved for issuance under our 2018 Equity Inducement Plan as of September 30, 2018;

- 1,759,602 additional shares of common stock reserved and available for future issuance under our 2016 Equity Incentive Plan as of October 8, 2018;

- 1,845,820 shares of common stock sold under our at-the-market program with JonesTrading Institutional Services LLC in October 2018, which we terminated in December 2018; and

- shares of our common stock that may be sold from time to time under an at-the-market program that we entered into in December 2018 with Jefferies LLC.

To the extent that outstanding options have been or may be exercised or other shares are issued, investors purchasing our common stock in this offering may experience further dilution. In addition, we may choose to issue additional common stock, or securities convertible into or exchangeable for common stock, in the future. The issuance of these securities could result in further dilution for investors purchasing our common stock in this offering.

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# Description of pre-funded warrants

The following is a brief summary of certain terms and conditions of the pre-funded warrants being offered by this prospectus supplement. The following description is subject in all respects to the provisions contained in the pre-funded warrants.

## Form

The pre-funded warrants will be issued as individual warrant agreements to the investors. The form of pre-funded warrant will be filed as an exhibit to our Current Report on Form 8-K that we expect to file with the SEC.

## Term

The pre-funded warrants will expire five years from the date of issuance.

## Exercisability

The pre-funded warrants are exercisable at any time after their original issuance until their expiration. The pre-funded warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice solely through a cashless exercise, in which the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the pre-funded warrant. No fractional shares of common stock will be issued in connection with the exercise of a pre-funded warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the last closing trading price of our common stock on the exercise date.

## Exercise limitations

Under the pre-funded warrants, we may not effect the exercise of any pre-funded warrant, and a holder will not be entitled to exercise any portion of any pre-funded warrant, which, upon giving effect to such exercise, would cause (i) the aggregate number of shares of our common stock beneficially owned by the holder (together with its affiliates) to exceed 4.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise, or (ii) the combined voting power of our securities beneficially owned by the holder (together with its affiliates) to exceed 4.99% of the combined voting power of all of our securities then outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. However, any holder may increase or decrease such percentage to any other percentage not in excess of 19.99% upon at least 61 days prior notice from the holder to us.

## Exercise price

The exercise price per whole share of our common stock purchasable upon the exercise of the pre-funded warrants is $0.0001 per share of common stock. The exercise price of the pre-funded warrants and the number of shares of our common stock issuable upon exercise of the pre-funded warrants is subject to appropriate adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock and also upon any distributions of assets, including cash, stock or other property to our stockholders. The exercise price will not be adjusted below the par value of our common stock.

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## Transferability

Subject to applicable laws, the pre-funded warrants may be offered for sale, sold, transferred or assigned without our consent.

## Exchange listing

We do not plan on applying to list the pre-funded warrants on The Nasdaq Global Market, any other national securities exchange or any other nationally recognized trading system.

## Fundamental transactions

In the event of a fundamental transaction, as described in the pre-funded warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding common stock, upon consummation of such a fundamental transaction, the holders of the pre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction without regard to any limitations on exercised contained in the pre-funded warrants.

## No rights as a stockholder

Except by virtue of such holder s ownership of shares of our common stock, the holder of a pre-funded warrant does not have the rights or privileges of a holder of our common stock, including any voting rights, until the holder exercises the pre-funded warrant.

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# Material United States federal income tax consequences for investors in our common stock and pre-funded warrants

The following summary describes the material U.S. federal income tax consequences of the acquisition, ownership and disposition of our common stock and pre-funded warrants acquired in this offering. This discussion does not address all aspects of U.S. federal income taxes, does not discuss the potential application of the alternative minimum tax or Medicare Contribution tax and does not deal with state or local taxes, U.S. federal gift and estate tax laws, except to the limited extent provided below, or any non-U.S. tax consequences that may be relevant to Non-U.S. Holders in light of their particular circumstances.

Special rules different from those described below may apply to certain investors that are subject to special treatment under the Internal Revenue Code of 1986, as amended, or Code, such as:

- insurance companies, banks and other financial institutions;
- tax-exempt organizations (including private foundations) and tax-qualified retirement plans;
- foreign governments and international organizations;
- broker-dealers and traders in securities;
- U.S. expatriates and certain former citizens or long-term residents of the United States;
- Non-U.S. Holders (as defined below) that own, or are deemed to own, more than 5% of our common stock (directly, indirectly or by attribution) or more than 5% of our pre-funded warrants;
- persons required for U.S. federal income tax purposes to conform the timing of income accruals to their financial statements under Section 451(b) of the Code;
- controlled foreign corporations, passive foreign investment companies and corporations that accumulate earnings to avoid U.S. federal income tax;
- persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or integrated investment or other risk reduction strategy;
- U.S. Holders (as defined below) whose functional currency for U.S. tax purposes is not the US dollar;
- 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); and

partnerships and other pass-through entities, and investors in such pass-through entities (regardless of their places of organization or formation).

Such investors are urged to consult their own tax advisors to determine the U.S. federal, state, local and other tax consequences that may be relevant to them.

Furthermore, the discussion below is based upon the provisions of the Code, and Treasury regulations, rulings and judicial decisions thereunder as of the date hereof, and such authorities may be repealed, revoked or modified, possibly retroactively, and are subject to differing interpretations which could result in U.S. federal income tax consequences different from those discussed below. We have not requested a ruling from the Internal Revenue Service, or IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions or will not take a contrary position regarding the tax consequences described herein, or that any such contrary position would not be sustained by a court.

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For the purposes of this discussion, a U.S. Holder means a beneficial owner of our common stock or pre-funded warrants, other than a partnership or other pass-through entity, that is for U.S. federal income tax purposes (a) an individual citizen or resident of the United States, (b) a corporation (or other entity taxable as a corporation for U.S. federal income tax purposes), created or organized in or under the laws of the United States, any state thereof or the District of Columbia, (c) an estate the income of which is subject to U.S. federal income taxation regardless of its source, or (d) a trust if it (1) is subject to the primary supervision of a court within the United States and one or more U.S. persons (within the meaning of Section 7701(a)(30) of the Code) have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person. A Non-U.S. Holder is, for U.S. federal income tax purposes, a beneficial owner of common stock or pre-funded warrants that is not a U.S. Holder or a partnership or other pass-through entity for U.S. federal income tax purposes.

If you are an individual non-U.S. citizen, you may, in some cases, be deemed to be 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. Generally, for this purpose, 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 generally subject to U.S. federal income tax as if they were U.S. citizens. Individuals who are uncertain of their status as resident or nonresident aliens for U.S. federal income tax purposes are urged to consult their own tax advisors regarding the U.S. federal income tax consequences of the ownership or disposition of our common stock.

PERSONS CONSIDERING THE PURCHASE OF OUR COMMON STOCK OR PRE-FUNDED WARRANTS PURSUANT TO THIS OFFERING SHOULD CONSULT THEIR OWN TAX ADVISORS CONCERNING THE U.S. FEDERAL INCOME TAX CONSEQUENCES OF ACQUIRING, OWNING AND DISPOSING OF OUR COMMON STOCK AND PRE-FUNDED WARRANTS IN LIGHT OF THEIR PARTICULAR SITUATIONS AS WELL AS ANY CONSEQUENCES ARISING UNDER THE LAWS OF ANY OTHER TAXING JURISDICTION, INCLUDING ANY STATE, LOCAL OR NON-U.S. TAX CONSEQUENCES OR ANY U.S. FEDERAL NON-INCOME TAX CONSEQUENCES, AND THE POSSIBLE APPLICATION OF TAX TREATIES.

## Tax treatment of the pre-funded warrants

We believe that our pre-funded warrants should be treated as our common stock for U.S. federal income tax purposes. However, our position is not binding on the IRS and the IRS may treat the pre-funded warrants as warrants to acquire our common stock and, if so, the amount and character of your gain with respect to an investment in our pre-funded warrants could change. Accordingly, you should consult your tax advisor regarding the U.S. federal tax consequences of an investment in the pre-funded warrants. The following discussion assumes our pre-funded warrants are properly treated as our common stock.

### *Tax consequences to U.S. Holders*

## Distributions on common stock or pre-funded warrants

We do not currently expect to make distributions on our common stock or pre-funded warrants. In the event that we do make distributions of cash or other property, distributions paid on common stock or pre-funded warrants will be treated as a dividend to the extent paid out of our current or accumulated earnings and profits, and will be includible in your income as ordinary income when received. However, with respect to dividends received by individuals, such dividends are generally taxed at the lower applicable long-term capital gains rates, provided certain holding period requirements are satisfied. Distributions in excess of our current and accumulated earnings and profits will be treated as a return of capital to the extent of a U.S. holder s tax basis

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in the common stock or pre-funded warrants and thereafter as capital gain from the sale or exchange of such common stock or pre-funded warrants. The tax treatment of such gain is further described in Sale or other disposition of common stock or pre-funded warrants below. Dividends received by a corporation may be eligible for a dividends received deduction, subject to applicable limitations.

### Sale or other disposition of common stock or pre-funded warrants

For U.S. federal income tax purposes, gain or loss realized on the sale or other disposition of common stock or pre-funded warrants will be capital gain or loss, and will be long-term capital gain or loss if you have held the common stock or pre-funded warrants for more than one year. The amount of the gain or loss will equal the difference between your tax basis in the common stock or pre-funded warrants disposed of and the amount realized on the disposition. Long-term capital gains recognized by non-corporate U.S. Holders will be subject to reduced tax rates. The deductibility of capital losses is subject to limitations.

### Exercise of pre-funded warrants

You will not be required to recognize income, gain or loss upon the exercise of a pre-funded warrant. Your tax basis in a share of common stock received upon exercise will be equal to the sum of (1) your tax basis in the pre-funded warrant and (2) the exercise price of the pre-funded warrant. Your holding period in the stock received upon exercise will include your holding period in the pre-funded warrants exchanged therefor.

### Information reporting and backup withholding

Information reporting requirements generally will apply to payments of dividends and gross proceeds on the sale or other disposition of our common stock and pre-funded warrants, unless the U.S. holder is an exempt recipient (such as a corporation). Backup withholding (currently at a 24% rate) will apply to those payments if the U.S. holder fails to provide its correct taxpayer identification number, or certification of exempt status, or if the U.S. holder is notified by the IRS that it has failed to report in full payments of interest and dividend income. Any amounts withheld under the backup withholding rules will be allowed as a refund or a credit against a U.S. holder s U.S. federal income tax liability provided the required information is furnished timely to the IRS.

## *Tax consequences to Non-U.S. Holders*

### Distributions on common stock or pre-funded warrants

We do not expect to make any distributions on our common stock or pre-funded warrants in the foreseeable future. If we do make distributions on our common stock or pre-funded warrants, however, such distributions made to a Non-U.S. Holder will constitute dividends for U.S. tax purposes to the extent paid out of 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 our common stock or pre-funded warrants. Any remaining excess will be treated as gain realized as described below under the section titled Sale or other disposition of common stock and pre-funded warrants.

Any distribution on our common stock or pre-funded warrants that is treated as a dividend paid to a Non-U.S. Holder that is not effectively connected with the holder s conduct of a trade or business in the United States will generally be subject to withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and the Non-U.S. Holder s country of residence. To obtain a

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reduced rate of withholding under a treaty, a Non-U.S. Holder generally will be required to provide the applicable withholding agent with a properly executed IRS Form W-8BEN, IRS Form W-8BEN-E or other appropriate form, certifying the Non-U.S. Holder s entitlement to benefits under that treaty. Such form must be provided prior to the payment of dividends and must be updated periodically. If a Non-U.S. Holder holds stock or pre-funded warrants through a financial institution or other agent acting on the holder s behalf, the holder will be required to provide appropriate documentation to such agent. The holder s agent may then be required to provide certification to the applicable withholding agent, either directly or through other intermediaries. If you are eligible for a reduced rate of U.S. withholding tax under an income tax treaty, you should consult with your own tax advisor to determine if you are able to obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS.

We generally are not required to withhold tax on dividends paid to a Non-U.S. Holder that are effectively connected with the holder s conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, are attributable to a permanent establishment that the holder maintains in the United States) if a properly executed IRS Form W-8ECI, stating that the dividends are so connected, is furnished to us (or, if stock or pre-funded warrants are held through a financial institution or other agent, to the applicable withholding agent). In general, such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular graduated rates applicable to U.S. persons, unless a specific treaty exemption applies. A corporate Non-U.S. Holder receiving effectively connected dividends may also be subject to an additional branch profits tax, which is imposed, under certain circumstances, at a rate of 30% (or such lower rate as may be specified by an applicable treaty) on the corporate Non-U.S. Holder s effectively connected earnings and profits, subject to certain adjustments.

See also the section below titled Foreign accounts for additional withholding rules that may apply to dividends paid to certain foreign financial institutions or non-financial foreign entities.

### Sale or other disposition of common stock and pre-funded warrants

Subject to the discussion below under the sections titled Backup withholding and information reporting, a Non-U.S. Holder generally will not be subject to U.S. federal income or withholding tax with respect to gain realized on a sale or other disposition of our common stock or pre-funded warrants unless (a) the gain is effectively connected with a trade or business of the holder in the United States (and, if required by an applicable income tax treaty, is attributable to a permanent establishment that the holder maintains in the United States), (b) the Non-U.S. Holder is a nonresident alien individual and is present in the United States for 183 or more days in the taxable year of the disposition and certain other conditions are met, or (c) we are or have been a United States real property holding corporation within the meaning of Code Section 897(c)(2) at any time within the shorter of the five-year period preceding such disposition or the holder s holding period in the common stock.

If you are a Non-U.S. Holder described in (a) above, you will be required to pay tax on the net gain derived from the sale at the regular graduated U.S. federal income tax rates applicable to U.S. persons, unless a specific treaty exemption applies. Corporate Non-U.S. Holders described in (a) above may also be subject to the additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. If you are an individual Non-U.S. Holder described in (b) above, you will be required to pay a flat 30% tax on the gain derived from the sale, which gain may be offset by certain U.S. source capital losses (even though you are not considered a resident of the United States), provided you have timely filed U.S. federal income tax returns with respect to such losses. With respect to (c) above, in general, we would be a U.S. real property holding corporation if interests in U.S. real estate comprised (by fair market value) at least half of our assets. We believe that we are not, and do not anticipate becoming, a U.S. real property holding corporation. However,

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there can be no assurance that we will not become a U.S. real property holding corporation in the future. Even if we are treated as a U.S. real property holding corporation, gain realized by a Non-U.S. Holder on a disposition of our common stock or pre-funded warrants will not be subject to U.S. federal income tax so long as (1) the Non-U.S. Holder owned, directly, indirectly or constructively, no more than five percent of our common stock and pre-funded warrants at all times within the shorter of (i) the five-year period preceding the disposition or (ii) the holder s holding period and (2) our common stock is regularly traded on an established securities market. There can be no assurance that our common stock will continue to qualify as regularly traded on an established securities market.

### Exercise of pre-funded warrants

You will not be required to recognize income, gain or loss upon the exercise of a pre-funded warrant.

### 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 and pre-funded warrants 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. The terms resident and nonresident are defined differently for U.S. federal estate tax purposes than for U.S. federal income tax purposes. Investors are urged to consult their own tax advisors regarding the U.S. federal estate tax consequences of the ownership or disposition of our common stock or pre-funded warrants.

### Backup withholding and information reporting

Generally, we or certain financial middlemen must report information to the IRS with respect to any dividends we pay on our common stock or pre-funded warrants including the amount of any such dividends, the name and address of the recipient, and the amount, if any, of tax withheld. A similar report is sent to the holder to whom any such dividends are paid. Pursuant to tax treaties or certain other agreements, the IRS may make its reports available to tax authorities in the recipient s country of residence.

Dividends paid by us (or our paying agents) to a Non-U.S. Holder may also be subject to U.S. backup withholding. U.S. backup withholding generally will not apply to a Non-U.S. Holder who provides a properly executed IRS Form W-8BEN or IRS Form W-8BEN-E, as applicable, or otherwise establishes an exemption, provided that the applicable withholding agent does not have actual knowledge or reason to know the holder is a U.S. person.

Under current U.S. federal income tax law, U.S. information reporting and backup withholding requirements generally will apply to the proceeds of a disposition of our common stock or pre-funded warrants effected by or through a U.S. office of any broker, U.S. or non-U.S., unless the Non-U.S. Holder provides a properly executed IRS Form W-8BEN or IRS Form W-8BEN-E, as applicable, or otherwise meets documentary evidence requirements for establishing non-U.S. person status or otherwise establishes an exemption. Generally, U.S. information reporting and backup withholding requirements will not apply to a payment of disposition proceeds to a Non-U.S. Holder where the transaction is effected outside the United States through a non-U.S. office of a non-U.S. broker. Information reporting and backup withholding requirements may, however, apply to a payment of disposition proceeds if the broker has actual knowledge, or reason to know, that the holder is, in fact, a U.S. person. For information reporting purposes, certain brokers with substantial U.S. ownership or operations will generally be treated in a manner similar to U.S. brokers.

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Backup withholding is not an additional tax. If backup withholding is applied to you, you should consult with your own tax advisor to determine whether you have overpaid your U.S. federal income tax, and whether you are able to obtain a tax refund or credit of the overpaid amount.

## Foreign accounts

In addition to, and separately from the withholding rules described above, U.S. federal withholding taxes may apply under the Foreign Account Tax Compliance Act, or FATCA, on certain types of payments, including dividends to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends paid in respect of our common stock or pre-funded warrants or the gross proceeds of the disposition on our common stock or pre-funded warrants paid to a foreign financial institution or a non-financial foreign entity (each as defined in the Code), unless (1) the foreign financial institution agrees to undertake certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any substantial United States owners (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. The 30% federal withholding tax described in this paragraph cannot be reduced under an income tax treaty with the United States. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain specified United States persons or United States-owned foreign entities (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules. Regulations proposed by the U.S. Department of the Treasury (which may be relied upon pending finalization) would eliminate the requirement of withholding on gross proceeds.

Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock.

EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK AND PRE-FUNDED WARRANTS, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAW, AS WELL AS TAX CONSEQUENCES ARISING UNDER ANY STATE, LOCAL, NON-U.S. OR U.S. FEDERAL NON-INCOME TAX LAWS SUCH AS ESTATE AND GIFT TAX.

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# Underwriting

We are offering the shares of common stock and pre-funded warrants described in this prospectus supplement through a number of underwriters. J.P. Morgan Securities LLC and Evercore Group L.L.C. are acting as joint book-running managers of the offering and as representatives of the underwriters. We expect to enter into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we will agree to sell to the underwriters, and each underwriter will severally agree to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus supplement, the number of shares of common stock and pre-funded warrants listed next to its name in the following table:

| Name | Number of shares | Number of pre-funded warrants |
|---|---|---|
| J.P. Morgan Securities LLC | | |
| Evercore Group L.L.C | | |
| H.C. Wainwright & Co. LLC | | |
| Total | | |

The underwriters are committed to purchase all the common shares and pre-funded warrants offered by us if they purchase any shares or pre-funded warrants. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the common shares and pre-funded warrants directly to the public at the initial public offering prices set forth on the cover page of this prospectus supplement and to certain dealers at those prices less a concession not in excess of $ per share. After the initial offering of the shares and pre-funded warrants to the public, if all of the common shares or pre-funded warrants are not sold at the initial public offering price, as the case may be, the underwriters may change the offering price and the other selling terms.

The underwriters have an option to buy up to additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The number of shares subject to the underwriters option will equal 15% of the total number of shares of common stock we are offering plus the shares underlying the pre-funded warrants. The underwriters have 30 days from the date of this prospectus supplement to exercise this option to purchase additional shares. If any shares are purchased with this option to purchase additional shares, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

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The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock, or the public offering price per pre-funded warrant less the amount paid by the underwriters to us per pre-funded warrant, as the case may be. The underwriting fee for the common stock is $ per share of common stock and the underwriting fee for each pre-funded warrant is $ . The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters option to purchase additional shares.

| | Without option to purchase additional shares exercise | With full option to purchase additional shares exercise |
|---|---|---|
| Per Share | | |
| Per Pre-Funded Warrant | | |
| Total | | |

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately $ . We also have agreed to reimburse the underwriters for certain of their expenses in an amount up to $20,000.

A prospectus supplement in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters 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 representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, or file with, or submit to, the Securities and Exchange Commission a registration statement under the Securities Act relating to, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition, submission or filing, or (ii) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock or any other such securities, whether any such transaction described in clause (i) or (ii) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, without the prior written consent of J.P. Morgan Securities LLC and Evercore Group L.L.C. for a period of 90 days after the date of this prospectus supplement. Such restrictions will not apply to (a) the shares of common stock and pre-funded warrants to be sold in this offering and the delivery of shares of our common stock pursuant to the exercise of the pre-funded warrants; (b) the issuance of shares of our common stock, stock option grants, the issuance of shares of our common stock underlying stock options and the issuance of other securities, in each case pursuant to a director or employee stock option plan, stock ownership plan or dividend reinvestment plan in effect on the date of the underwriting agreement; (c) the issuance of shares of our common stock pursuant to the conversion or the exercise of securities that are outstanding on the date of the underwriting agreement; (d) the entry into agreements providing for the issuance by us of shares of our common stock or any security convertible into or exercisable for shares of our common stock in connection with the acquisition by us or by any of our subsidiaries of the securities, business, property or other assets of another person or entity pursuant to an employee benefit plan that we assume in connection with such acquisition, and the issuance of any such securities pursuant to any such agreement; (e) the entry into agreements providing for the issuance of shares of our common stock or any security convertible into or exercisable for shares of our common stock in connection

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with joint ventures, commercial relationships or other strategic transactions, and the issuance of any such securities pursuant to any such agreements; *provided that* in the case of clauses (d) and (e), the aggregate number of shares of our common stock that we may sell or issue or agree to sell or issue shall not exceed 5.0% of the total number of shares of our common stock issued and outstanding immediately subsequent to the completion of the transactions contemplated by this offering; *provided further* that in the case of clauses (d) and (e), it shall be a condition to the sale, issuance or transfer of shares of any such securities that the transferee executes and delivers a lock-up agreement to the representatives; (f) the adoption of a new equity incentive plan, the filing of a registration statement on Form S-8 under the Securities Act to register the offer and sale of securities to be issued pursuant to such new equity incentive plan, and the issuance of securities pursuant to such new equity incentive plan or any other employee benefit or equity incentive plan as of the date of the underwriting agreement; and (g) file amendments to, and request effectiveness of, the registration statement on Form S-3 (Registration No. 333-228967) previously filed with the Commission on December 21, 2018.

In addition, each of our directors and executive officers have entered into lock-up agreements with the underwriters pursuant to which each of these persons may not, for a period of 90 days after the date of this prospectus supplement, without the prior written consent of J.P. Morgan Securities LLC and Evercore Group L.L.C., (1) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors and executive officers in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant), (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock. These lockup agreements are subject to certain exceptions, including: (a) certain gifts and certain transfers by will or intestate succession; (b) if the party is affiliated with a corporation, partnership, limited liability company, or other business entity, any transfers by such corporation, partnership, limited liability company or other business entity to any current or former stockholder, partner or member of, or owner of a similar equity interest in, the undersigned, as the case may be, if such transfer is not for value; (c) any transfer made by a corporation, partnership, limited liability company or other business entity to another corporation, partnership, limited liability company or other business entity so long as the transferee is an affiliate of such corporation, partnership, limited liability company or other business entity and such transfer is not for value; (d) if the party holds our securities in a trust, transfers to the settlor or beneficiary of a trust or to the estate of a beneficiary of such trust; (e) transactions relating to (x) shares of common stock acquired in this offering and (y) shares of common stock or other securities convertible into or exercisable or exchangeable for common stock acquired in open market transactions after completion of this offering, *provided* that no filing under Section 16(a) of the Securities Exchange Act of 1934, as amended (the Exchange Act ) is made in connection with such transactions; (f) transfers of shares of our common stock to us pursuant to agreements under which we have the option to repurchase shares upon termination of service or a right of first refusal with respect to the transfer of such shares; (g) the establishment of a 10b5-1 trading plan providing for the sale of common stock, *provided* that such plan does not provide for, or permit, the sale of any common stock during the 90-day lock-up period and no public announcement or filing is made regarding such plan during the 90-day lock-up period; (h) any transfers made to us to satisfy tax withholding obligations in connection with the vesting or exercise of equity awards granted pursuant to our equity incentive plans disclosed in this prospectus

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supplement; (i) transfers pursuant to a bona fide third-party tender offer, merger, consolidation, binding share exchange or other similar transaction involving a change of control of us; *provided that* if such transaction is not consummated, such securities held by the lock-up party will remain subject to the lock-up agreement; (j) any 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; (k) the exercise of any option, warrant or other right to acquire shares of our common stock, the settlement of any stock-settled stock appreciation rights, restricted stock or restricted stock units, including through transfers to us in connection with a net or cashless exercise, in each case granted and outstanding as of the date of the lock-up agreement or at the closing date of this offering; and (l) the sale or transfer of shares of common stock beneficially owned after the date that is 60 days after the date of the underwriting agreement, *provided* that the aggregate number of such beneficially owned shares that may be sold or transferred by all of our directors and executive officers pursuant to this clause (l) may not exceed an aggregate of 1% of the total issued and outstanding shares of our common stock immediately after the consummation of this offering, and provided further that in the case of any transfer described in clauses (a), (b), (c), (d), (i) and (j), the transferee agrees in writing to be bound by the lockup restrictions.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

Our common stock is quoted on The Nasdaq Global Market under the symbol AGLE . The pre-funded warrants will not be listed on any national securities exchange.

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be covered shorts, which are short positions in an amount not greater than the underwriters option to purchase additional shares referred to above, or may be naked shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option to purchase additional shares. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act of 1933, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of our common stock, and, as a result, the price of our common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on the Nasdaq Global Market, in the over-the-counter market or otherwise.

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In addition, in connection with this offering certain of the underwriters (and selling group members) may engage in passive market making transactions in our common stock on The Nasdaq Global Market prior to the pricing and completion of this offering. Passive market making consists of displaying bids on The Nasdaq Global Market no higher than the bid prices of independent market makers and making purchases at prices no higher than these independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are generally limited to a specified percentage of the passive market maker s average daily trading volume in the common stock during a specified period and must be discontinued when such limit is reached. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the absence of these transactions. If passive market making is commenced, it may be discontinued at any time.

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

## Selling restrictions

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus supplement in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement may not be offered or sold, directly or indirectly, nor may this prospectus supplement or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement. This prospectus supplement does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement in any jurisdiction in which such an offer or a solicitation is unlawful.

***European Economic Area***

In relation to each Member State of the European Economic Area (each, a Relevant Member State ), no offer of securities may be made to the public in that Relevant Member State other than:

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

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

C. in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of securities shall require the Company or the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

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Each person in a Relevant Member State who initially acquires any securities or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a qualified investor within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any securities being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the securities acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any securities to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

The Company, the representatives and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus has been prepared on the basis that any offer of securities in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of securities. Accordingly any person making or intending to make an offer in that Relevant Member State of the securities which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the Company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the Company nor the underwriters have authorized, nor do they authorize, the making of any offer of securities in circumstances in which an obligation arises for the Company or the underwriters to publish a prospectus for such offer.

For the purpose of the above provisions, the expression an offer to the public in relation to any 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 the securities, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression Prospectus Directive means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) and includes any relevant implementing measure in the Relevant Member State and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

***United Kingdom***

In the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are qualified investors (as defined in the Prospectus Directive) (i) 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, as amended (the Order ) and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as relevant persons ).

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this document or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

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***Bermuda***

Securities may be offered or sold in Bermuda only in compliance with the provisions of the Investment Business Act of 2003 of Bermuda which regulates the sale of securities in Bermuda. Additionally, non-Bermudian persons (including companies) may not carry on or engage in any trade or business in Bermuda unless such persons are permitted to do so under applicable Bermuda legislation.

***Australia***

This prospectus:

- does not constitute a product disclosure document or a prospectus under Chapter 6D.2 of the Corporations Act 2001 (Cth) (the Corporations Act );
- has not been, and will not be, lodged with the Australian Securities and Investments Commission ( ASIC ), as a disclosure document for the purposes of the Corporations Act and does not purport to include the information required of a disclosure document under Chapter 6D.2 of the Corporations Act;
- does not constitute or involve a recommendation to acquire, an offer or invitation for issue or sale, an offer or invitation to arrange the issue or sale, or an issue or sale, of interests to a retail client (as defined in section 761G of the Corporations Act and applicable regulations) in Australia; and
- may only be provided in Australia to select investors who are able to demonstrate that they fall within one or more of the categories of investors, or Exempt Investors, available under section 708 of the Corporations Act.

These securities may not be directly or indirectly offered for subscription or purchased or sold, and no invitations to subscribe for or buy the securities may be issued, and no draft or definitive offering memorandum, advertisement or other offering material relating to any securities may be distributed in Australia, except where disclosure to investors is not required under Chapter 6D of the Corporations Act or is otherwise in compliance with all applicable Australian laws and regulations. By submitting an application for the securities, you represent and warrant to us that you are an Exempt Investor.

As any offer of securities under this prospectus will be made without disclosure in Australia under Chapter 6D.2 of the Corporations Act, the offer of those securities for resale in Australia within 12 months may, under section 707 of the Corporations Act, require disclosure to investors under Chapter 6D.2 if none of the exemptions in section 708 applies to that resale. By applying for the securities you undertake to us that you will not, for a period of 12 months from the date of issue of the securities, offer, transfer, assign or otherwise alienate those securities to investors in Australia except in circumstances where disclosure to investors is not required under Chapter 6D.2 of the Corporations Act or where a compliant disclosure document is prepared and lodged with ASIC.

***Hong Kong***

These securities have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to professional investors as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a prospectus as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to these securities has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong

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Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to these securities which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

***Japan***

These securities have not been and will not be registered pursuant to Article 4, Paragraph 1 of the Financial Instruments and Exchange Act. Accordingly, none of the securities nor any interest therein may be offered or sold, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to or for the benefit of a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Act and any other applicable laws, regulations and ministerial guidelines of Japan in effect at the relevant time.

***Singapore***

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of these securities may not be circulated or distributed, nor may these securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA ), (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where our securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is: (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares of our common stock pursuant to an offer made under Section 275 of the SFA except:

- to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- where no consideration is or will be given for the transfer;
- where the transfer is by operation of law;
- as specified in Section 276(7) of the SFA; or
- as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

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***Switzerland***

These securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange ( SIX ) or on any other stock exchange or regulated trading facility in Switzerland. This document does not constitute a prospectus within the meaning of, and has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to our securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company, or our securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of shares of our common stock has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes ( CISA ). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of our securities.

***Canada***

These 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 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) 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.

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# Legal matters

The validity of the common stock offered hereby and certain legal matters in connection with this offering will be passed upon by Fenwick & West LLP, Mountain View, California. Certain legal matters with respect to the securities offered hereby will be passed upon for the underwriters by Davis Polk & Wardwell LLP, Menlo Park, California.

# Experts

The financial statements incorporated in this prospectus supplement by reference to the Annual Report on Form 10-K for the year ended December 31, 2017 have been so incorporated 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.

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# Where you can find more information

We have filed with the SEC a registration statement on Form S-3 under the Securities Act with respect to the securities offered hereby. This prospectus supplement, 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 securities offered hereby, reference is made to the accompanying prospectus and registration statement of which it is a part and the exhibits filed therewith. Statements contained in this prospectus supplement regarding the contents of any contract or any other document that is filed as an exhibit to the accompanying prospectus and the registration statement of which it is a part 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 or the exhibits to the reports or other documents incorporated by reference in this prospectus for a copy of such contract or other document.

We are subject to the informational requirements of the Exchange Act and are required to file annual, quarterly and other reports, proxy statements and other information with the SEC. The SEC maintains an Internet site (http://www.sec.gov) that contains reports, proxy and information statements, and various other information about us. You may also inspect the documents described herein at our principal executive offices, 901 S. MoPac Expressway, Barton Oaks Plaza One, Suite 250, Austin, TX 78746, during normal business hours.

Information about us is also available at our website at http://www.aegleabio.com. However, the information on our website is not a part of this prospectus supplement and is not incorporated by reference into this prospectus supplement.

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# Incorporation of information by reference

The SEC allows us to incorporate by reference information that we file with the SEC, which means that we can disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus supplement and the accompanying prospectus, and information we file later with the SEC will automatically update and supersede this information. A Current Report (or portion thereof) furnished, but not filed, on Form 8-K shall not be incorporated by reference into this prospectus supplement and the accompanying prospectus. We incorporate by reference the documents listed below and any future filings we make with the SEC under Section 13(a), 13(c), 14, or 15(d) of the Exchange Act prior to the termination of any offering of securities made by this prospectus supplement and accompanying prospectus:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2017 filed with the SEC on March 13, 2018, including certain information incorporated by reference therein from our Definitive Proxy Statement for our 2018 annual meeting of stockholders filed with the SEC on April 16, 2018;

- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2018, June 30, 2018 and September 30, 2018, filed with the SEC on May 8, 2018, August 9, 2018 and November 8, 2018, respectively;

- our Current Reports on Form 8-K filed on March 26, 2018, April 16, 2018, April 19, 2018, June 8, 2018, July 16, 2018, July 23, 2018, October 10, 2018, November 29, 2018 and December 21, 2018 (in each case, except for information contained therein which is furnished rather than filed); and

- the description of our common stock contained in our registration statement on Form 8-A filed with the SEC on March 28, 2016 under Section 12 of the Exchange Act, including any amendment or report filed for the purpose of updating such description.

We will furnish without charge to you, on written or oral request, a copy of any or all of such documents that has been incorporated herein by reference (other than exhibits to such documents unless such exhibits are specifically incorporated by reference into the documents that this prospectus incorporates). Written or oral requests for copies should be directed Aeglea BioTherapeutics, Inc., Attn: Investor Relations, 901 S. MoPac Expressway, Barton Oaks Plaza One, Suite 250, Austin, Texas 78746, telephone number (512) 942-2935. See the section of this prospectus supplement entitled Where you can find more information for information concerning how to read and obtain copies of materials that we file with the SEC at the SEC s public offices.

Any statement contained in this prospectus supplement, or in a document all or a portion of which is incorporated by reference, shall be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement or any document incorporated by reference modifies or supersedes such statement. Any such statement so modified or superseded shall not, except as so modified or superseded, constitute a part of this prospectus.

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**PROSPECTUS**

**$150,000,000**

**Aeglea BioTherapeutics, Inc.**

**Common Stock, Preferred Stock,**

**Debt Securities, Warrants, Subscription Rights and Units**

From time to time, we may offer up to $150,000,000 aggregate dollar amount of shares of our common stock or preferred stock, debt securities, warrants to purchase our common stock, preferred stock or debt securities, subscription rights to purchase our common stock, preferred stock or debt securities and/or units consisting of some or all of these securities, in any combination, together or separately, in one or more offerings, in amounts, at prices and on the terms that we will determine at the time of the offering and which will be set forth in a prospectus supplement and any related free writing prospectus. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. The total amount of these securities will have an initial aggregate offering price of up to $150,000,000.

You should read this prospectus, the information incorporated, or deemed to be incorporated, by reference in this prospectus, and any applicable prospectus supplement and related free writing prospectus carefully before you invest.

Our common stock is traded on The NASDAQ Global Market under the symbol AGLE. On April 28, 2017 the last reported sales price for our common stock was $7.15 per share. None of the other securities we may offer are currently traded on any securities exchange. The applicable prospectus supplement and any related free writing prospectus will contain information, where applicable, as to any other listing on The NASDAQ Global Market or any securities market or exchange of the securities covered by the prospectus supplement and any related free writing prospectus.

**An investment in our securities involves a high degree of risk. You should carefully consider the information under the heading Risk Factors beginning on page 6 of this prospectus before investing in our securities.**

Common stock, preferred stock, debt securities, warrants, subscription rights and/or units may be sold by us to or through underwriters or dealers, directly to purchasers or through agents designated from time to time. For additional information on the methods of sale, you should refer to the section entitled Plan of Distribution in this prospectus. If any underwriters, dealers or agents are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such underwriters or agents and any applicable fees, discounts or commissions, details regarding over-allotment options, if any, and the net proceeds to us will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

**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.**

**The date of this prospectus is May 30, 2017**

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## ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a shelf registration process. Under this shelf registration process, from time to time, we may sell any combination of the securities described in this prospectus in one or more offerings, up to a total dollar amount of $150,000,000. We have provided to you in this prospectus a general description of the securities we may offer. Each time we sell securities under this shelf registration process, we will provide a prospectus supplement that will contain specific information about the terms of the offering. We may also add, update or change in the prospectus supplement any of the information contained in this prospectus. To the extent there is a conflict between the information contained in this prospectus and the prospectus supplement, you should rely on the information in the prospectus supplement; *provided* that, if any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in this prospectus or any prospectus supplement the statement in the document having the later date modifies or supersedes the earlier statement. You should read both this prospectus and any prospectus supplement together with additional information described under the next heading Where You Can Find More Information.

You should rely only on the information contained in or incorporated by reference into this prospectus or any applicable prospectus supplement. No dealer, salesperson or any other person is authorized to give any information or to make any representation other than the information and representations contained in or incorporated by reference into this prospectus or any applicable prospectus supplement. If different information is given or different representations are made, you may not rely on that information or those representations as having been authorized by us. You may not imply from the delivery of this prospectus and any applicable prospectus supplement, nor from a sale made under this prospectus and any applicable prospectus supplement, that our affairs are unchanged since the date of this prospectus and any applicable prospectus supplement or that the information contained in any document incorporated by reference is accurate as of any date other than the date of the document incorporated by reference, regardless of the time of delivery of this prospectus and any applicable prospectus supplement or any sale of a security. This prospectus and any applicable prospectus supplement may only be used where it is legal to sell the securities.

***THIS PROSPECTUS MAY NOT BE USED TO OFFER AND SELL SECURITIES UNLESS IT IS ACCOMPANIED BY AN ADDITIONAL PROSPECTUS OR A PROSPECTUS SUPPLEMENT.***

In this prospectus, unless the context otherwise requires, the terms Aeglea, the Company, we, us, and our refer t Aeglea BioTherapeutics, Inc., a Delaware corporation, and its consolidated subsidiaries.

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## PROSPECTUS SUMMARY

This summary may not contain all the information that you should consider before investing in securities. You should read the entire prospectus and the information incorporated by reference in this prospectus carefully, including Risk Factors and the financial data and related notes and other information incorporated by reference, before making an investment decision.

### Company Overview

We are a biotechnology company committed to developing enzyme-based therapeutics in the field of amino acid metabolism to treat rare genetic diseases and cancer. Our engineered human enzymes are designed to degrade specific amino acids in the blood to target these diseases. In inborn errors of metabolism, or IEM, a subset of rare genetic diseases, we are seeking to reduce the toxic levels of amino acids in patients to the normal range. 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 (pegzilarginase), 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 clinical proof of mechanism in both scenarios. In a Phase 1 clinical trial for the treatment of patients with Arginase I deficiency, a dose-proportional reduction in plasma arginine levels was observed in two patients. A reduction in blood arginine levels was also observed in Phase 1 clinical trials for the treatment of patients with advanced solid tumors and the hematological malignancies relapsed refractory acute myeloid leukemia, or AML, and myelodysplastic syndrome, or MDS. These preliminary results support AEB1102 s potential use as a therapeutic of both Arginase I deficiency and certain cancers associated with abnormal amino acid metabolism.

We are conducting three clinical trials for AEB1102, consisting of one Phase 1/2 clinical trial for the treatment of Arginase I deficiency and two Phase 1 clinical trials for the treatment of certain cancers.

**Arginase I Deficiency.** Following completion of dosing for the first two adult patients in our Phase 1 clinical trial for the treatment of patients with Arginase I deficiency, we submitted a protocol amendment in November 2016 to broaden the scope of our Phase 1 trial into a Phase 1/2 trial. The amended protocol includes dosing of pediatric patients (two and older) and weekly repeat dosing, with the intent to assess the safety, tolerability, pharmacokinetics, pharmacodynamics, and clinical response of AEB1102 in patients with this IEM. In the first quarter of 2017, we received IRB approval for the Phase 1/2 protocol for the treatment of patients with Arginase I deficiency at multiple clinical trial sites. In March 2017, we received an information request from the FDA which included comments and recommendations on the protocol amendment and a request for supporting documents based on their review of our completed toxicology studies, our dose escalation plan and our information to support the inclusion of pediatric patients. As recommended by the FDA, we replied with supporting information and completed a follow-up meeting. Based on discussions with the FDA, we were unable to resolve a difference in opinion at this time on the data needed to support inclusion of pediatric patients, which has resulted in a delay in our plan to initiate dosing in pediatric patients in the United States. We anticipate continuing our dialogue with the FDA on this topic and will continue to focus on our Phase 1/2 trial, which we expect to begin enrolling adult patients in the middle of 2017. Results from the first two adult patients in our Phase 1 clinical trial for the treatment of Arginase I deficiency were announced at the 2017 American College of Medical Genetics and Genomics

Annual Clinical Genetics Meeting in March 2017.

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**Advanced Solid Tumors.** In October 2015, we initiated enrollment for a Phase 1 dose escalation trial for cancer patients with advanced solid tumors. In this ongoing trial, patients have demonstrated a reduction in blood arginine levels from the dosing of AEB1102, providing proof-of-mechanism. We expect to announce results of this Phase 1 dose escalation in patients with advanced solid tumors and anticipate initiating expansion arms in specific solid tumor types, potentially in combination with existing or emerging standards of care, in the fourth quarter of 2017 or the first quarter of 2018.

**Hematological Malignancies.** In July 2016, we initiated a Phase 1 clinical trial in patients with the hematological malignancies AML and MDS in the United States and Canada. As demonstrated in the trial for patients with advanced solid tumors, the first three cohorts of this trial have demonstrated proof-of-mechanism. We expect to announce results of the Phase 1 dose escalation trial in patients with AML and MDS in the fourth quarter of 2017 or the first quarter of 2018.

Our pipeline of engineered human enzyme product candidates in preclinical development includes: AEB3103, an enzyme that degrades the amino acid cysteine, and its oxidized form cystine, to target a widely recognized, but previously underexploited 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 homocysteine. We plan to continue preclinical development of AEB3103, AEB2109, AEB4104 and related variants of these candidates with the aim of submitting an IND for one or more of these development candidates in 2018.

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.

**The Securities We May Offer**

With this prospectus, we may offer common stock, preferred stock, debt securities, warrants, subscription rights to purchase our common stock, preferred stock or debt securities, and/or units consisting of some or all of these securities in any combination. The aggregate offering price of securities that we offer with this prospectus will not exceed $150,000,000. Each time we offer securities with this prospectus, we will provide offerees with a prospectus supplement that will contain the specific terms of the securities being offered. The following is a summary of the securities we may offer with this prospectus.

*Common Stock*

We may offer shares of our common stock, par value $0.0001 per share.

*Preferred Stock*

We may offer shares of our preferred stock, par value $0.0001 per share, in one or more series. Our board of directors or a committee designated by the board will determine the dividend, voting, conversion and other rights of the series of shares of preferred stock being offered. Each series of preferred stock will be more fully described in the particular prospectus supplement that will accompany this prospectus, including redemption provisions, rights in the event of our liquidation, dissolution or the winding up, voting rights and rights to convert into common stock.

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*Debt Securities*

We may offer general obligations, which may be secured or unsecured, senior or subordinated and convertible into shares of our common stock or preferred stock. In this prospectus, we refer to the senior debt securities and the subordinated debt securities together as the debt securities. Our board of directors will determine the terms of each series of debt securities being offered.

We will issue the debt securities under an indenture between us and a trustee. In this document, we have summarized general features of the debt securities from the indenture. We encourage you to read the indenture, which is an exhibit to the registration statement of which this prospectus is a part.

*Warrants*

We may offer warrants for the purchase of debt securities, shares of preferred stock or shares of common stock. We may issue warrants independently or together with other securities. Our board of directors will determine the terms of the warrants.

*Subscription Rights*

We may offer subscription rights for the purchase of common stock, preferred stock or debt securities. We may issue subscription rights independently or together with other securities. Our board of directors will determine the terms of the subscription rights.

*Units*

We may offer units consisting of some or all of the securities described above, in any combination, including common stock, preferred stock, warrants and/or debt securities. The terms of these units will be set forth in a prospectus supplement. The description of the terms of these units in the related prospectus supplement will not be complete. You should refer to the applicable form of unit and unit agreement for complete information with respect to these units.

* * *

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 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. We have research and development operations and corporate offices in Austin, TX.

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## RATIO OF EARNINGS TO FIXED CHARGES

The following table sets forth our dollar coverage deficiency. The ratio of earnings to fixed charges is not disclosed since it is a negative number in each year and period shown below. Any time we offer debt securities pursuant to this prospectus, we will provide an updated table setting forth our ratio of earnings to fixed charges on a historical basis in the applicable prospectus supplement, if required. Any time we offer shares of preferred stock pursuant to this prospectus, we will provide a table setting forth our ratio of combined fixed charges and preferred stock dividends to earnings, if required.

| | Period From December 16, 2013 (Inception) to December 31, 2013 | Year Ended December 31, 2014 | Year Ended December 31, 2015 | Year Ended December 31, 2016 |
|---|---|---|---|---|
| | (1) | (1) | (1) | (1) |

(1) Due to our net losses for the periods presented earnings were insufficient to cover fixed charges. For this reason, no ratios are provided.

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## RISK FACTORS

An investment in our securities involves a high degree of risk. The prospectus supplement applicable to each offering of securities will contain a discussion of the risks applicable to an investment in our securities. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading Risk Factors in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under Part I, Item 1A, Risk Factors, in our Annual Report on Form 10-K for the year ended December 31, 2016, which is incorporated herein by reference, and may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations.

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## FORWARD-LOOKING STATEMENTS

This prospectus and documents incorporated herein by reference contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements involve a number of risks and uncertainties. We caution readers that any forward-looking statement is not a guarantee of future performance and that actual results could differ materially from those contained in the forward-looking statement. These statements are based on current expectations of future events. Such statements include, but are not limited to, statements about future financial and operating results, plans, objectives, expectations and intentions, costs and expenses, outcome of contingencies, financial condition, results of operations, liquidity, cost savings, objectives of management, business strategies, debt financing, timing and plans for our nonclinical studies and clinical trials, the achievement of clinical and commercial milestones, the advancement of our technologies and our proprietary product candidates, and other statements that are not historical facts. You can find many of these statements by looking for words like believes, expects, anticipates, estimates, may, might, should, will, could, plan, intend similar expressions in this prospectus or in documents incorporated by reference into this prospectus. We intend that such forward-looking statements be subject to the safe harbors created thereby.

These forward-looking statements are based on the current beliefs and expectations of our management and are subject to significant risks and uncertainties. If underlying assumptions prove inaccurate or unknown risks or uncertainties materialize, actual results may differ materially from current expectations and projections. Factors that might cause such a difference include those discussed in Part I, Item 1A Risk Factors in our Annual Report on Form 10-K for the year ended December 31, 2016, as well as those discussed in this prospectus and in the documents incorporated by reference into this prospectus. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this prospectus or, in the case of documents referred to or incorporated by reference, the date of those documents.

All subsequent written or oral forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section. We do not undertake any obligation to release publicly any revisions to these forward-looking statements to reflect events or circumstances after the date of this prospectus or to reflect the occurrence of unanticipated events, except as may be required under applicable U.S. securities law. If we do update one or more forward-looking statements, no inference should be drawn that we will make additional updates with respect to those or other forward-looking statements.

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## WHERE YOU CAN FIND MORE INFORMATION

We are subject to the informational requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act and are required to file annual, quarterly and other reports, proxy statements and other information with the SEC. You may inspect and copy these reports, proxy statements and other information at the public reference facilities maintained by the SEC in Washington, D.C., 100 F Street N.E., Washington, D.C. 20549. Copies of such materials can be obtained from the SEC s public reference section at prescribed rates. You may obtain information on the operation of the public reference rooms by calling the SEC at (800) SEC-0330. Additionally, the SEC maintains an Internet site (http://www.sec.gov) that contains reports, proxy and information statements, and various other information about us. You may also inspect the documents described herein at our principal executive offices, 901 S. MoPac Expressway, Barton Oaks Plaza One, Suite 250, Austin, TX 78746, during normal business hours.

Information about us is also available at our website at http://www.aegleabio.com. However, the information on our website is not a part of this prospectus and is not incorporated by reference into this prospectus.

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## INCORPORATION OF INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference information that we file with the SEC, which means that we can disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus, and information we file later with the SEC will automatically update and supersede this information. A Current Report (or portion thereof) furnished, but not filed, on Form 8-K shall not be incorporated by reference into this prospectus. We incorporate by reference the documents listed below and any future filings we make with the SEC under Section 13(a), 13(c), 14, or 15(d) of the Exchange Act prior to the termination of any offering of securities made by this prospectus:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2016 filed with the SEC on March 23, 2017, including certain information incorporated by reference therein from our Definitive Proxy Statement for our 2017 annual meeting of stockholders filed with the SEC on April 21, 2017;

- our Quarterly Report on Form 10-Q for the quarter ended March 31, 2017, filed with the SEC on May 9, 2017;

- our Current Report on Form 8-K filed on February 16, 2017;

- the description of our common stock contained in our registration statement on Form 8-A filed with the SEC on March 28, 2016 under Section 12 of the Exchange Act, including any amendment or report filed for the purpose of updating such description; and

- filings we make with the SEC pursuant to the Exchange Act after the date of the initial registration statement, of which this prospectus is a part, and prior to the effectiveness of the registration statement.

We will furnish without charge to you, on written or oral request, a copy of any or all of such documents that has been incorporated herein by reference (other than exhibits to such documents unless such exhibits are specifically incorporated by reference into the documents that this prospectus incorporates). Written or oral requests for copies should be directed Aeglea BioTherapeutics, Inc., Attn: Investor Relations, 901 S. MoPac Expressway, Barton Oaks Plaza One, Suite 250, Austin, Texas 78746, telephone number (512) 942-2935. See the section of this prospectus entitled Where You Can Find More Information for information concerning how to read and obtain copies of materials that we file with the SEC at the SEC s public offices.

Any statement contained in this prospectus, or in a document all or a portion of which is incorporated by reference, shall be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus, any prospectus supplement or any document incorporated by reference modifies or supersedes such statement. Any such statement so modified or superseded shall not, except as so modified or superseded, constitute a part of this prospectus.

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## USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds to us from the sale of our securities under this prospectus. Unless otherwise provided in the applicable prospectus supplement, we intend to use the net proceeds from the sale of securities under this prospectus for general corporate purposes, which may include funding research and development, increasing our working capital, reducing indebtedness, acquisitions or investments in businesses, products or technologies that are complementary to our own and capital expenditures. We will set forth in the prospectus supplement our intended use for the net proceeds received from the sale of any securities. Pending the application of the net proceeds, we intend to invest the net proceeds in short-term or long-term, investment-grade, interest-bearing securities.

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## PLAN OF DISTRIBUTION

We may sell the securities covered by this prospectus to one or more underwriters for public offering and sale by them, and may also sell the securities to investors directly or through agents. We will name any underwriter or agent involved in the offer and sale of securities in the applicable prospectus supplement. We have reserved the right to sell or exchange securities directly to investors on our own behalf in jurisdictions where we are authorized to do so. We may distribute the securities from time to time in one or more transactions:

at a fixed price or prices, which may be changed;

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

We may directly solicit offers to purchase the securities being offered by this prospectus. We may also designate agents to solicit offers to purchase the securities from time to time. We will name in a prospectus supplement any agent involved in the offer or sale of our securities. Unless otherwise indicated in a prospectus supplement, an agent will be acting on a best efforts basis, and a dealer will purchase securities as a principal for resale at varying prices to be determined by the dealer.

If we utilize an underwriter in the sale of the securities being offered by this prospectus, we will execute an underwriting agreement with the underwriter at the time of sale and we will provide the name of any underwriter in the prospectus supplement that the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we, or the purchasers of securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters or commissions from the purchasers for whom they may act as agent.

We will provide in the applicable prospectus supplement any compensation we pay to underwriters, dealers, or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act of 1933, as amended, or the Securities Act, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, and to reimburse them for certain expenses. We may grant underwriters who participate in the distribution of our securities under this prospectus an option to purchase additional securities to cover any over-allotments in connection with the distribution.

The securities we offer under this prospectus may or may not be listed through The NASDAQ Global Market or any other securities exchange. To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include short sales of the securities, which involves the sale by persons participating in the offering of more securities than we sold

to them. In these circumstances, these persons would cover such short positions by making purchases in the open market or by exercising their option to purchase additional securities. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

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We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and they may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in these sale transactions will be an underwriter and will be identified in the applicable prospectus supplement. In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus. The financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

We will file a prospectus supplement to describe the terms of any offering of our securities covered by this prospectus. The prospectus supplement will disclose:

- the terms of the offer;
- the names of any underwriters, including any managing underwriters, as well as any dealers or agents;
- the purchase price of the securities from us;
- the net proceeds to us from the sale of the securities;
- any delayed delivery arrangements;
- any over-allotment or other options under which underwriters, if any, may purchase additional securities from us;
- any underwriting discounts, commissions or other items constituting underwriters compensation, and any commissions paid to agents;
- in a subscription rights offering, whether we have engaged dealer-managers to facilitate the offering or subscription, including their name or names and compensation;
- any public offering price; and

other facts material to the transaction.

We will bear all or substantially all of the costs, expenses and fees in connection with the registration of our securities under this prospectus. The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

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## DESCRIPTION OF CAPITAL STOCK

### General

Our authorized capital stock consists 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, which are included as exhibits to the registration statement of which this prospectus forms a part, and to the applicable provisions of Delaware law.

As of March 31, 2017, there were 13,452,260 shares of our common stock outstanding, and no shares of preferred stock outstanding.

### 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. For more information about our dividend policy, see Dividend Policy in our Annual Report on Form 10-K for the year ended December 31, 2016, which is incorporated by reference in this prospectus.

*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 holders of a majority of the shares of our common stock are able to elect all of our directors. Our restated certificate of incorporation establishes a classified board of directors, 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

Our board of directors is 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

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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.

**Registration Rights**

Pursuant to the terms of our investors rights agreement entered into in March 2015, certain of our common stock holders are entitled to rights with respect to the registration of their shares under the Securities Act, as described below. We refer to these shares collectively as registrable securities.

*Demand registration rights*

The holders of at least 62% of the shares of common stock issued upon the conversion of Series B convertible preferred stock in connection with our initial public offering 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 common stock that were issued upon the conversion of shares of preferred stock in connection with our initial public offering 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.

*Piggyback registration rights*

If we register any of our securities for public sale in an offering pursuant to this prospectus, 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, 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.

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*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 our initial public offering, or when that holder ceases to hold such registrable securities.

**Anti-Takeover Provisions**

The provisions of Delaware law, our restated certificate of incorporation and our restated bylaws 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:

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;

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

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.

**Restated Certificate of Incorporation and Restated Bylaw Provisions**

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

***Board of Directors vacancies.*** Our restated certificate of incorporation and restated bylaws 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 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.

***Classified board.*** Our restated certificate of incorporation and restated bylaws 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.

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***Stockholder action; special meetings of stockholders.*** Our restated certificate of incorporation provides 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 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.

***Advance notice requirements for stockholder proposals and director nominations.*** Our restated bylaws 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 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 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.

***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 do not provide for cumulative voting.

***Directors removed only for cause.*** Our restated certificate of incorporation provides that stockholders may remove directors only for cause.

***Amendment of charter provisions.*** Any amendment of the above provisions in our restated certificate of incorporation requires 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.

***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 enables 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.

***Choice of forum.*** Our restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is 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**

The transfer agent and registrar for our common stock is American Stock Transfer and Trust Company, LLC. The transfer agent s address is 6201 15th Avenue, Brooklyn, New York 11219, and its telephone number is (800) 937-5449.

**Exchange Listing**

Our common stock is listed on The NASDAQ Global Market under the symbol AGLE.

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## DESCRIPTION OF DEBT SECURITIES

### General

We will issue the debt securities offered by this prospectus and any accompanying prospectus supplement under an indenture to be entered into between us and the trustee identified in the applicable prospectus supplement. The terms of the debt securities will include those stated in the indenture and those made part of the indenture by reference to the Trust Indenture Act of 1939, as in effect on the date of the indenture. We have filed a copy of the form of indenture as an exhibit to the registration statement in which this prospectus is included. The indenture will be subject to and governed by the terms of the Trust Indenture Act of 1939.

We may offer under this prospectus up to an aggregate principal amount of $150,000,000 in debt securities, or if debt securities are issued at a discount, or in a foreign currency, foreign currency units or composite currency, the principal amount as may be sold for an aggregate public offering price of up to $150,000,000. Unless otherwise specified in the applicable prospectus supplement, the debt securities will represent our direct, unsecured obligations and will rank equally with all of our other unsecured indebtedness.

We may issue the debt securities in one or more series with the same or various maturities, at par, at a premium, or at a discount. We will describe the particular terms of each series of debt securities in a prospectus supplement relating to that series, which we will file with the SEC. The prospectus supplement relating to the particular series of debt securities being offered will specify the particular amounts, prices and terms of those debt securities. These terms may include:

- the title of the series;
- the aggregate principal amount, and, if a series, the total amount authorized and the total amount outstanding;
- the issue price or prices, expressed as a percentage of the aggregate principal amount of the debt securities;
- any limit on the aggregate principal amount;
- the date or dates on which principal is payable;
- the interest rate or rates (which may be fixed or variable) or, if applicable, the method used to determine such rate or rates;
- the date or dates from which interest, if any, will be payable and any regular record date for the interest payable;

the place or places where principal and, if applicable, premium and interest, is payable;

the terms and conditions upon which we may, or the holders may require us to, redeem or repurchase the debt securities;

the denominations in which such debt securities may be issuable, if other than denominations of $1,000 or any integral multiple of that number;

whether the debt securities are to be issuable in the form of certificated securities (as described below) or global securities (as described below);

the portion of principal amount that will be payable upon declaration of acceleration of the maturity date if other than the principal amount of the debt securities;

the currency of denomination;

the designation of the currency, currencies or currency units in which payment of principal and, if applicable, premium and interest, will be made;

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if payments of principal and, if applicable, premium or interest, on the debt securities are to be made in one or more currencies or currency units other than the currency of denomination, the manner in which the exchange rate with respect to such payments will be determined;

if amounts of principal and, if applicable, premium and interest may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index, then the manner in which such amounts will be determined;

the provisions, if any, relating to any collateral provided for such debt securities;

any addition to or change in the covenants and/or the acceleration provisions described in this prospectus or in the indenture;

any events of default, if not otherwise described below under Events of Default ;

the terms and conditions, if any, for conversion into or exchange for shares of our common stock or preferred stock;

any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents; and

the terms and conditions, if any, upon which the debt securities shall be subordinated in right of payment to our other indebtedness.

We may issue discount debt securities that provide for an amount less than the stated principal amount to be due and payable upon acceleration of the maturity of such debt securities in accordance with the terms of the indenture. We may also issue debt securities in bearer form, with or without coupons. If we issue discount debt securities or debt securities in bearer form, we will describe material U.S. federal income tax considerations and other material special considerations which apply to these debt securities in the applicable prospectus supplement.

We may issue debt securities denominated in or payable in a foreign currency or currencies or a foreign currency unit or units. If we do, we will describe the restrictions, elections, and general tax considerations relating to the debt securities and the foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Debt securities offered under this prospectus and any prospectus supplement will be subordinated in right of payment to certain of our outstanding senior indebtedness. In addition, we will seek the consent of the holders of any such senior indebtedness prior to issuing any debt securities under this prospectus to the extent required by the agreements evidencing such senior indebtedness.

**Registrar and Paying Agent**

The debt securities may be presented for registration of transfer or for exchange at the corporate trust office of the security registrar or at any other office or agency that we maintain for those purposes. In addition, the debt securities may be presented for payment of principal, interest and any premium at the office of the paying agent or at any office or agency that we maintain for those purposes.

**Conversion or Exchange Rights**

Debt securities may be convertible into or exchangeable for shares of our common stock. The terms and conditions of conversion or exchange will be stated in the applicable prospectus supplement. The terms will include, among others, the following:

the conversion or exchange price;

the conversion or exchange period;

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provisions regarding the convertibility or exchangeability of the debt securities, including who may convert or exchange;

events requiring adjustment to the conversion or exchange price;

provisions affecting conversion or exchange in the event of our redemption of the debt securities; and

any anti-dilution provisions, if applicable.

**Registered Global Securities**

If we decide to issue debt securities in the form of one or more global securities, then we will register the global securities in the name of the depositary for the global securities or the nominee of the depositary, and the global securities will be delivered by the trustee to the depositary for credit to the accounts of the holders of beneficial interests in the debt securities.

The prospectus supplement will describe the specific terms of the depositary arrangement for debt securities of a series that are issued in global form. None of us, the trustee, any payment agent or the security registrar will have any responsibility or liability for any aspect of the records relating to or payments made on account of beneficial ownership interests in a global debt security or for maintaining, supervising or reviewing any records relating to these beneficial ownership interests.

**No Protection in the Event of Change of Control**

The indenture does not have any covenants or other provisions providing for a put or increased interest or otherwise that would afford holders of our debt securities additional protection in the event of a recapitalization transaction, a change of control or a highly leveraged transaction. If we offer any covenants or provisions of this type with respect to any debt securities covered by this prospectus, we will describe them in the applicable prospectus supplement.

**Covenants**

Unless otherwise indicated in this prospectus or the applicable prospectus supplement, our debt securities will not have the benefit of any covenants that limit or restrict our business or operations, the pledging of our assets or the incurrence by us of indebtedness. We will describe in the applicable prospectus supplement any material covenants in respect of a series of debt securities.

**Merger, Consolidation or Sale of Assets**

The form of indenture provides that we will not consolidate with or merge into any other person or convey, transfer, sell or lease our properties and assets substantially as an entirety to any person, unless:

we are the surviving person of such merger or consolidation, or if we are not the surviving person, the person formed by the consolidation or into or with which we are merged or the person to which our properties and assets are conveyed, transferred, sold or leased, is a corporation organized and existing under the laws of the

U.S., any state or the District of Columbia or a corporation or comparable legal entity organized under the laws of a foreign jurisdiction and has expressly assumed all of our obligations, including the payment of the principal of and, premium, if any, and interest on the debt securities and the performance of the other covenants under the indenture; and

immediately before and immediately after giving effect to the transaction on a pro forma basis, no event of default, and no event which, after notice or lapse of time or both, would become an event of default, has occurred and is continuing under the indenture.

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**Events of Default**

Unless otherwise specified in the applicable prospectus supplement, the following events will be events of default under the indenture with respect to debt securities of any series:

- we fail to pay any principal or premium, if any, when it becomes due;
- we fail to pay any interest within 30 days after it becomes due;
- we fail to observe or perform any other covenant in the debt securities or the indenture for 60 days after written notice specifying the failure from the trustee or the holders of not less than 25% in aggregate principal amount of the outstanding debt securities of that series; and
- certain events involving bankruptcy, insolvency or reorganization of us or any of our significant subsidiaries.

The trustee may withhold notice to the holders of the debt securities of any series of any default, except in payment of principal of or premium, if any, or interest on the debt securities of a series, if the trustee considers it to be in the best interest of the holders of the debt securities of that series to do so.

If an event of default (other than an event of default resulting from certain events of bankruptcy, insolvency or reorganization) occurs, and is continuing, then the trustee or the holders of not less than 25% in aggregate principal amount of the outstanding debt securities of any series may accelerate the maturity of the debt securities. If this happens, the entire principal amount, plus the premium, if any, of all the outstanding debt securities of the affected series plus accrued interest to the date of acceleration will be immediately due and payable. At any time after the acceleration, but before a judgment or decree based on such acceleration is obtained by the trustee, the holders of a majority in aggregate principal amount of outstanding debt securities of such series may rescind and annul such acceleration if:

- all events of default (other than nonpayment of accelerated principal, premium or interest) have been cured or waived;
- all lawful interest on overdue interest and overdue principal has been paid; and
- the rescission would not conflict with any judgment or decree.

In addition, if the acceleration occurs at any time when we have outstanding indebtedness that is senior to the debt securities, the payment of the principal amount of outstanding debt securities may be subordinated in right of payment to the prior payment of any amounts due under the senior indebtedness, in which case the holders of debt securities will be entitled to payment under the terms prescribed in the instruments evidencing the senior indebtedness and the indenture.

If an event of default resulting from certain events of bankruptcy, insolvency or reorganization occurs, the principal, premium and interest amount with respect to all of the debt securities of any series will be due and payable immediately without any declaration or other act on the part of the trustee or the holders of the debt securities of that series.

The holders of a majority in principal amount of the outstanding debt securities of a series will have the right to waive any existing default or compliance with any provision of the indenture or the debt securities of that series and to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, subject to certain limitations specified in the indenture.

No holder of any debt security of a series will have any right to institute any proceeding with respect to the indenture or for any remedy under the indenture, unless:

the holder gives to the trustee written notice of a continuing event of default;

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the holders of at least 25% in aggregate principal amount of the outstanding debt securities of the affected series make a written request and offer reasonable indemnity to the trustee to institute a proceeding as trustee;

the trustee fails to institute a proceeding within 60 days after such request; and

the holders of a majority in aggregate principal amount of the outstanding debt securities of the affected series do not give the trustee a direction inconsistent with such request during such 60-day period.

These limitations do not, however, apply to a suit instituted for payment on debt securities of any series on or after the due dates expressed in the debt securities.

We will periodically deliver certificates to the trustee regarding our compliance with our obligations under the indenture.

**Modification and Waiver**

From time to time, we and the trustee may, without the consent of holders of the debt securities of one or more series, amend the indenture or the debt securities of one or more series, or supplement the indenture, for certain specified purposes, including:

to provide that the surviving entity following a change of control permitted under the indenture will assume all of our obligations under the indenture and debt securities;

to provide for certificated debt securities in addition to uncertificated debt securities;

to comply with any requirements of the SEC under the Trust Indenture Act of 1939;

to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;

to cure any ambiguity, defect or inconsistency, or make any other change that does not materially and adversely affect the rights of any holder; and

to appoint a successor trustee under the indenture with respect to one or more series.

From time to time we and the trustee may, with the consent of holders of at least a majority in principal amount of an outstanding series of debt securities, amend or supplement the indenture or the debt securities series, or waive compliance in a particular instance by us with any provision of the indenture or the debt securities. We may not, however, without the consent of each holder affected by such action, modify or supplement the indenture or the debt securities or waive compliance with any provision of the indenture or the debt securities in order to:

reduce the amount of debt securities whose holders must consent to an amendment, supplement, or waiver to the indenture or such debt security;

reduce the rate of or change the time for payment of interest or reduce the amount of or postpone the date for payment of sinking fund or analogous obligations;

reduce the principal of or change the stated maturity of the debt securities;

make any debt security payable in money other than that stated in the debt security;

change the amount or time of any payment required or reduce the premium payable upon any redemption, or change the time before which no such redemption may be made;

waive a default in the payment of the principal of, premium, if any, or interest on the debt securities or a redemption payment;

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waive a redemption payment with respect to any debt securities or change any provision with respect to redemption of debt securities; or

take any other action otherwise prohibited by the indenture to be taken without the consent of each holder affected by the action.

**Defeasance of Debt Securities and Certain Covenants in Certain Circumstances**

The indenture permits us, at any time, to elect to discharge our obligations with respect to one or more series of debt securities by following certain procedures described in the indenture. These procedures will allow us either:

to defease and be discharged from any and all of our obligations with respect to any debt securities except for the following obligations (which discharge is referred to as legal defeasance ):

1. to register the transfer or exchange of such debt securities;

2. to replace temporary or mutilated, destroyed, lost or stolen debt securities;

3. to compensate and indemnify the trustee; or

4. to maintain an office or agency in respect of the debt securities and to hold monies for payment in trust; or

to be released from our obligations with respect to the debt securities under certain covenants contained in the indenture, as well as any additional covenants which may be contained in the applicable supplemental indenture (which release is referred to as covenant defeasance ).

In order to exercise either defeasance option, we must irrevocably deposit with the trustee or other qualifying trustee, in trust for that purpose:

money;

U.S. Government Obligations (as described below) or Foreign Government Obligations (as described below) that through the scheduled payment of principal and interest in accordance with their terms will provide money; or

a combination of money and/or U.S. Government Obligations and/or Foreign Government Obligations sufficient in the written opinion of a nationally-recognized firm of independent accountants to provide

money;

that, in each case specified above, provides a sufficient amount to pay the principal of, premium, if any, and interest, if any, on the debt securities of the series, on the scheduled due dates or on a selected date of redemption in accordance with the terms of the indenture.

In addition, defeasance may be effected only if, among other things:

in the case of either legal or covenant defeasance, we deliver to the trustee an opinion of counsel, as specified in the indenture, stating that as a result of the defeasance neither the trust nor the trustee will be required to register as an investment company under the Investment Company Act of 1940;

in the case of legal defeasance, we deliver to the trustee an opinion of counsel stating that we have received from, or there has been published by, the Internal Revenue Service a ruling to the effect that, or there has been a change in any applicable federal income tax law with the effect that (and the opinion shall confirm that), the holders of outstanding debt securities will not recognize income, gain or loss for U.S. federal income tax purposes solely as a result of such legal defeasance and will be subject to U.S. federal income tax on the same amounts, in the same manner, including as a result of prepayment, and at the same times as would have been the case if legal defeasance had not occurred;

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in the case of covenant defeasance, we deliver to the trustee an opinion of counsel to the effect that the holders of the outstanding debt securities will not recognize income, gain or loss for U.S. federal income tax purposes as a result of covenant defeasance and will be subject to U.S. federal income tax on the same amounts, in the same manner and at the same times as would have been the case if covenant defeasance had not occurred; and

certain other conditions described in the indenture are satisfied.

If we fail to comply with our remaining obligations under the indenture and applicable supplemental indenture after a covenant defeasance of the indenture and applicable supplemental indenture, and the debt securities are declared due and payable because of the occurrence of any undefeased event of default, the amount of money and/or U.S. Government Obligations and/or Foreign Government Obligations on deposit with the trustee could be insufficient to pay amounts due under the debt securities of the affected series at the time of acceleration. We will, however, remain liable in respect of these payments.

The term U.S. Government Obligations as used in the above discussion means securities that are direct obligations of or non-callable obligations guaranteed by the United States of America for the payment of which obligation or guarantee the full faith and credit of the United States of America is pledged.

The term Foreign Government Obligations as used in the above discussion means, with respect to debt securities of any series that are denominated in a currency other than U.S. dollars, (1) direct obligations of the government that issued or caused to be issued such currency for the payment of which obligations its full faith and credit is pledged or (2) obligations of a person controlled or supervised by or acting as an agent or instrumentality of such government the timely payment of which is unconditionally guaranteed as a full faith and credit obligation by that government, which in either case under clauses (1) or (2), are not callable or redeemable at the option of the issuer.

**Regarding the Trustee**

We will identify the trustee with respect to any series of debt securities in the prospectus supplement relating to the applicable debt securities. You should note that if the trustee becomes a creditor of ours, the indenture and the Trust Indenture Act of 1939 limit the rights of the trustee to obtain payment of claims in certain cases, or to realize on certain property received in respect of any such claim, as security or otherwise. The trustee and its affiliates may engage in, and will be permitted to continue to engage in, other transactions with us and our affiliates. If, however, the trustee acquires any conflicting interest within the meaning of the Trust Indenture Act of 1939, it must eliminate such conflict or resign.

The holders of a majority in principal amount of the then outstanding debt securities of any series may direct the time, method and place of conducting any proceeding for exercising any remedy available to the trustee. If an event of default occurs and is continuing, the trustee, in the exercise of its rights and powers, must use the degree of care and skill of a prudent person in the conduct of his or her own affairs. Subject to that provision, the trustee will be under no obligation to exercise any of its rights or powers under the indenture at the request of any of the holders of the debt securities, unless they have offered to the trustee reasonable indemnity or security.

**No Individual Liability of Incorporators, Stockholders, Officers or Directors**

Each indenture provides that no incorporator and no past, present or future stockholder, officer or director of our company or any successor corporation in those capacities will have any individual liability for any of our obligations, covenants or agreements under the debt securities or such indenture.

**Governing Law**

The indentures and the debt securities will be governed by, and construed in accordance with, the laws of the State of New York.

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## DESCRIPTION OF WARRANTS

### General

We may issue warrants for the purchase of our debt securities, preferred stock, common stock, or any combination thereof. Warrants may be issued independently or together with our debt securities, preferred stock or common stock and may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a bank or trust company, as warrant agent. The warrant agent will act solely as our agent in connection with the warrants. The warrant agent will not have any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants. This summary of certain provisions of the warrants is not complete. For the terms of a particular series of warrants, you should refer to the prospectus supplement for that series of warrants and the warrant agreement for that particular series.

### Debt Warrants

The prospectus supplement relating to a particular issue of warrants to purchase debt securities will describe the terms of the debt warrants, including the following:

- the title of the debt warrants;
- the offering price for the debt warrants, if any;
- the aggregate number of the debt warrants;
- the designation and terms of the debt securities, including any conversion rights, purchasable upon exercise of the debt warrants;
- if applicable, the date from and after which the debt warrants and any debt securities issued with them will be separately transferable;
- the principal amount of debt securities that may be purchased upon exercise of a debt warrant and the exercise price for the warrants, which may be payable in cash, securities or other property;
- the dates on which the right to exercise the debt warrants will commence and expire;
- if applicable, the minimum or maximum amount of the debt warrants that may be exercised at any one time;

whether the debt warrants represented by the debt warrant certificates or debt securities that may be issued upon exercise of the debt warrants will be issued in registered or bearer form;

information with respect to book-entry procedures, if any;

the currency or currency units in which the offering price, if any, and the exercise price are payable;

if applicable, a discussion of material U.S. federal income tax considerations;

the antidilution provisions of the debt warrants, if any;

the redemption or call provisions, if any, applicable to the debt warrants;

any provisions with respect to the holder s right to require us to repurchase the debt warrants upon a change in control or similar event; and

any additional terms of the debt warrants, including procedures and limitations relating to the exchange, exercise, and settlement of the debt warrants.

Debt warrant certificates will be exchangeable for new debt warrant certificates of different denominations. Debt warrants may be exercised at the corporate trust office of the warrant agent or any other office indicated in

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the prospectus supplement. Prior to the exercise of their debt warrants, holders of debt warrants will not have any of the rights of holders of the debt securities purchasable upon exercise and will not be entitled to payment of principal or any premium, if any, or interest on the debt securities purchasable upon exercise.

**Equity Warrants**

The prospectus supplement relating to a particular series of warrants to purchase our common stock or preferred stock will describe the terms of the warrants, including the following:

- the title of the warrants;
- the offering price for the warrants, if any;
- the aggregate number of warrants;
- the designation and terms of the common stock or preferred stock that may be purchased upon exercise of the warrants;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each security;
- if applicable, the date from and after which the warrants and any securities issued with the warrants will be separately transferable;
- the number of shares of common stock or preferred stock that may be purchased upon exercise of a warrant and the exercise price for the warrants;
- the dates on which the right to exercise the warrants shall commence and expire;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- if applicable, a discussion of material U.S. federal income tax considerations;

the antidilution provisions of the warrants, if any;

the redemption or call provisions, if any, applicable to the warrants;

any provisions with respect to a holder s right to require us to repurchase the warrants upon a change in control or similar event; and

any additional terms of the warrants, including procedures and limitations relating to the exchange, exercise and settlement of the warrants.

Holders of equity warrants will not be entitled:

to vote, consent, or receive dividends;

receive notice as stockholders with respect to any meeting of stockholders for the election of our directors or any other matter; or

exercise any rights as stockholders.

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## DESCRIPTION OF SUBSCRIPTION RIGHTS

We may issue subscription rights to purchase our common stock, preferred stock or debt securities. These subscription rights may be offered independently or together with any other security offered hereby and may or may not be transferable by the stockholder receiving the subscription rights in such offering. In connection with any offering of subscription rights, we may enter into a standby arrangement with one or more underwriters or other purchasers pursuant to which the underwriters or other purchasers may be required to purchase any securities remaining unsubscribed for after such offering.

The prospectus supplement relating to any subscription rights we offer, if any, will, to the extent applicable, include specific terms relating to the offering, including some or all of the following:

- the price, if any, for the subscription rights;
- the exercise price payable for our common stock, preferred stock or debt securities upon the exercise of the subscription rights;
- the number of subscription rights to be issued to each stockholder;
- the number and terms of our common stock, preferred stock or debt securities which may be purchased per each subscription right;
- the extent to which the subscription rights are transferable;
- any other terms of the subscription rights, including the terms, procedures and limitations relating to the exchange and exercise of the subscription rights;
- the date on which the right to exercise the subscription rights shall commence, and the date on which the subscription rights shall expire;
- the extent to which the subscription rights may include an over-subscription privilege with respect to unsubscribed securities or an over-allotment privilege to the extent the securities are fully subscribed; and
- if applicable, the material terms of any standby underwriting or purchase arrangement which may be entered into by us in connection with the offering of subscription rights.

The description in the applicable prospectus supplement of any subscription rights we offer will not necessarily be complete and will be qualified in its entirety by reference to the applicable subscription rights certificate, which will be filed with the SEC if we offer subscription rights. We urge you to read the applicable subscription rights certificate

and any applicable prospectus supplement in their entirety.

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## DESCRIPTION OF UNITS

We may issue units consisting of some or all of the securities described above, in any combination, including common stock, preferred stock, warrants and/or debt securities. The terms of these units will be set forth in a prospectus supplement. The description of the terms of these units in the related prospectus supplement will not be complete. You should refer to the applicable form of unit and unit agreement for complete information with respect to these units.

## LEGAL MATTERS

Fenwick & West LLP, Mountain View, California, will issue an opinion about certain legal matters with respect to the securities. Any underwriters or agents will be advised about legal matters relating to any offering by their own counsel.

## EXPERTS

The financial statements incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2016 have been so incorporated 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.

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***$50,000,000***

***Common stock***

***Pre-funded warrants to purchase common stock***

*Joint Book-Running Managers*

**J.P. Morgan** **Evercore ISI**

*Lead Manager*

**H.C. Wainwright & Co.**