Aeglea BioTherapeutics, Inc.
Form 424B5
April 17, 2018
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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 APRIL 17, 2018

PRELIMINARY PROSPECTUS SUPPLEMENT

(To Prospectus dated May 30, 2017)

4,500,000 Shares

Aeglea BioTherapeutics, Inc.

Common Stock

We are offering 4,500,000 shares of our common stock. Our common stock is quoted on The Nasdaq Global Market under the symbol AGLE. On April 16, 2018, the last reported sales price for our common stock was $9.01 per share.

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. You should carefully consider the information under the heading Risk Factors beginning on page S-7 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement before you invest in our securities.

	Per Share	Total
Public offering price	$	$
Underwriting discounts and commissions[(1)]	$	$
Proceeds to Aeglea BioTherapeutics, Inc. (before expenses)	$	$

(1) See Underwriting in this prospectus supplement for additional information regarding the compensation payable to the underwriters.

We have granted the underwriters an option for a period of 30 days to purchase up to an additional 675,000 shares of our common stock.

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

Delivery of the shares of common stock is expected to be made on or about , 2018.

Joint Book-Running Managers

Evercore ISI **BMO Capital Markets**

Lead Manager

JonesTrading

Prospectus Supplement dated , 2018

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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 only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the offering of the common stock 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 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 corpor and its subsidiaries, taken as a whole, unless otherwise 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, including the risk factors and the financial statements and related notes included or incorporated by reference herein and therein.

Company Overview

We are a clinical-stage 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 over bacterial enzyme-based approaches including a more favorable safety profile that may provide a greater likelihood of clinical success.

Our capabilities in enzyme engineering, preclinical disease modelling, 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
- 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 Development Programs

Pegzilarginase Overview

Our lead product candidate, pegzilarginase, is an enhanced human arginase that enzymatically degrades the amino acid arginine. Pegzilarginase is a recombinant, human Arginase 1 enzyme with modifications that enhance the stability and arginine-degrading activity of the enzyme in human plasma, and we believe it has a lower likelihood of immunogenicity in patients than bacterial arginine-degrading enzymes. Our lead program, pegzilarginase is in early

clinical development for two indications.

1. Arginase 1 Deficiency, which is a rare progressive autosomal recessive metabolic disease caused by a marked decrease in the activity of the native arginase 1 enzyme, which plays a key role in the degradation of arginine as part of the urea cycle.

2. Arginine dependent cancers, which demonstrate a vulnerability that leads to an increased dependency on extracellular arginine.

Pegzilarginase in Rare Genetic Disease

Phase 1/2 Open-Label Study of Pegzilarginase in Patients with Arginase 1 Deficiency: We are conducting a Phase 1/2 clinical trial for the treatment of patients with Arginase 1 Deficiency to assess the safety and clinical activity of pegzilarginase. The Phase 1/2, multi-center, single-arm, open-label trial of pegzilarginase is expected

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to enroll approximately 10 adult and pediatric patients with Arginase 1 Deficiency in the United States, and potentially in Canada and Europe. The trial investigates both single ascending doses (Part 1) and repeated dosing (Part 2). The primary endpoint of the trial is safety and tolerability of intravenous administration of pegzilarginase in patients with Arginase 1 Deficiency. The trial also will evaluate the pharmacokinetic and pharmacodynamic effects of repeated doses of pegzilarginase on plasma arginine levels, as well as clinical activity of pegzilarginase after repeated doses. Additionally, patients who complete the repeat dose part of the Phase 1/2 trial are eligible to enroll in a long-term open label extension study.

In April 2018, we announced preliminary data that confirmed the utility of standardized assessment tools in quantifying disease manifestations and that we believe demonstrates clinically relevant treatment effects with pegzilarginase in two Arginase 1 Deficiency patients after eight weeks of dosing. Baseline data in five patients indicated that clinical abnormalities in Arginase 1 Deficiency patients can be detected and quantified using standardized assessment tools. Assessment tools used in the trial include:

- Six-Minute Walk Test (6MWT) was below age and gender match norms for all five patients
- Berg Balance Scale demonstrated impaired balance in two patients
- Gross Motor Function Measure (GMFM) total and Part E subscale (walking, running, and jumping) was abnormal in four of the five patients
- Purdue Pegboard test demonstrated fine motor ability was also quantifiably impaired in all five patients
- All five patients had markedly elevated plasma arginine and plasma guanidino compounds (GC)
- All patients had evidence of growth impairment with height in the lowest 10% for age and gender and protein intakes less than the prescribed restricted amounts, which we believe likely reflects an aversion to protein caused by the disease
- One patient had abnormal baseline ammonia and hepatic transaminases, which are also potentially important disease related biochemical manifestations
- Tests of neurocognition were abnormal in all subjects indicating significant cognitive impairment

Data was available for the first two patients that we believe demonstrated clinically relevant treatment effects using standardized assessment tools:

6MWT demonstrated that two patients observed improvements on pegzilarginase. Patient 1 experienced a 31.4% improvement, from 102 to 134 meters, and Patient 2 experienced a 23.4% improvement, from 261 to 322 meters. Both observed improvements were well above the Minimal Clinically Important Difference (MCID) of 9% at eight weeks, with continued improvement, described above, measured at twenty weeks.

Berg Balance Scale measured a clinically meaningful improvement in balance in Patient 1, who transitioned from a high risk to a medium risk of fall category. Patient 2 had a normal baseline assessment which precluded demonstration of any improvement.

The GMFM Part E subscale demonstrated clinically important improvement after the initial eight repeat doses with further improvement by twenty weeks in Patient 1. Patient 2 was already at the upper end of the scale and, as expected, no significant change was observed.

Protein intake relative to the prescribed amount improved during the initial eight weeks of repeat dosing in the first two patients. Despite the increase in protein intake, patients plasma arginine values were better controlled with pegzilarginase as compared to baseline values with a protein restricted diet and ammonia scavengers.

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In March 2018, we announced repeat dose data from the two adults who had completed Part 2 of the study and single dose data from the first pediatric patient dosed in Part 1. Repeat doses of 0.04 mg/kg of pegzilarginase resulted in marked and sustained reductions in plasma arginine levels with accompanying reductions in other guanidino compounds, which are metabolites of arginine. Single and repeated doses of pegzilarginase in the two adult patients were well-tolerated with no serious adverse events or infusion-associated reactions with both subjects completing all their scheduled infusions. The only related adverse events reported included mild pruritis and mild dry skin. Pegzilarginase was well tolerated with the exception of a single infusion-associated reaction in one patient who had anti-drug antibodies (ADA) and blunting of the expected reduction in plasma arginine after the second dose. Three related serious adverse events of facial flushing, facial swelling, and throat tightness were reported in this pediatric patient after the second infusion. After dose interruption, treatment was completed with medication and rate adjustment without further adverse events. The patient transitioned to the repeat dose part of the trial and received three further infusions. Although dosing was well-tolerated with medication and rate adjustment with mild related adverse events of weakness, mood change, stomach ache, and pallor, the patient withdrew consent due to personal reasons. No marked or sustained increase in ADA titers were seen in the two adult Arginase 1 Deficiency patients or in the 40 advanced solid tumor patients tested after dosing with pegzilarginase. Baseline ADA at low titer was detected in one of two adult Arginase 1 Deficiency patients and five of 40 cancer patients. There was no apparent effect of the presence of the ADA on arginine reduction or safety profile.

We expect to report additional pediatric and adult repeat dose data in patients with Arginase 1 Deficiency in the third quarter of 2018. To date, we have identified more than 100 patients who have Arginase 1 Deficiency worldwide.

Phase 1/2 Open-Label Extension Study to Evaluate the Long-Term Safety, Tolerability and Effects of Pegzilarginase in Patients with Arginase 1 Deficiency Who Received Treatment in a Previous Study: After completing the repeat dose portion of the Phase 1/2 study and at least four weeks of post-treatment observation, patients may continue treatment with pegzilarginase by enrolling in a long-term open-label extension study. This study is expected to provide important insights into the longer term clinical effects of reducing plasma arginine. In December 2017, we announced the initiation of this study with the recruitment of two adult patients who had previously completed the repeat dose phase (Part 2) of the previous study. No related adverse events have been reported in this study as of April 8, 2018.

Regulatory Designations: We have obtained orphan drug designation from the FDA and EMA, as well as Fast Track Designation from the FDA, for pegzilarginase for the treatment of patients with Arginase 1 Deficiency. If the data from our Phase 1/2 trial is supportive, we may seek to accelerate our development plan for pegzilarginase by requesting to use established regulatory pathways, such as Breakthrough Therapy Designation. Regardless of whether we receive this designation, we anticipate initiating a pivotal trial of 20 to 40 patients and, if successful, we expect that this trial would support registration filing in the US and Europe.

Pegzilarginase in Cancer

Phase 1 Dose Escalation Trial of Pegzilarginase in Patients with Advanced Solid Tumors: In October 2015, we initiated the Phase 1 open label, multiple dose, dose escalation clinical trial in patients with advanced solid tumors. The primary objective of dose-escalation is to determine the maximum tolerated dose, and secondary objectives are to evaluate the safety, tolerability, and pharmacokinetic profile of pegzilarginase. The inclusion criteria include patients with locally advanced or metastatic solid tumors that failed to respond to or progressed under standard treatment, could not tolerate standard therapies, or for which no standard therapy exists.

In December 2017, we reported topline results of the dose escalation trial in which 40 patients were enrolled. The maximum tolerated dose was established at 0.33 mg/kg weekly by intravenous infusion, based on observations of reversible rash and reversible tremor at 0.40 mg/kg/week. Two dose-limiting toxicities (DLT) were observed: failure

to thrive and maculopapular rash. Other treatment-related serious or Grade 3/4 adverse events (AEs) that

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were not DLTs per protocol, including those that occurred after the DLT window, were hypophosphatemia, anemia (developed from a Grade 1 baseline), neutropenia (developed from a Grade 1 baseline), tremor, weakness, and transient hypertension. Treatment-related AEs in 10% or more of patients included nausea, stomatitis/mouth sores, fatigue, vomiting, rash, decreased appetite, and diarrhea, which were primarily Grades 1 or 2. Other serious adverse events, including death, occurred on study but were not considered related to pegzilarginase treatment. Most patients discontinued due to disease progression, and only one patient discontinued due to an adverse event that was considered related to pegzilarginase (tremor). Clinical proof of mechanism was demonstrated, with a rapid and sustained reduction of plasma arginine to levels substantially less than the normal range in cancer patients. Additionally, preliminary evidence suggesting clinical activity was observed in two out of nine patients with forms of melanoma who had stable disease longer than 12 weeks while receiving pegzilarginase.

In the first quarter of 2018, we initiated recruitment to cohort expansions of approximately 12 patients each and dosed our first patients with SCLC, uveal melanoma and cutaneous melanoma. The primary endpoint of each cohort expansion is to assess the safety of pegzilarginase in patients with each tumor type. Secondary endpoints include the assessment of pharmacokinetics, pharmacodynamics and clinical response. We will also use the data to inform the viability of companion diagnostic development, which has the potential to enrich patient populations with the greatest likelihood of clinical success.

Phase 1/2 Combination Trial in SCLC: 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 to explore the correlation of tumor expression of ASS1 and PD-L1 with clinical activity, as well as immunoprofiling of tumor samples, circulating cytokines, and immune cells. We dosed the first patient in the first quarter of 2018, expect to initiate Phase 2 in the third quarter of 2018, and expect to report topline safety and clinical activity for Phase 1 in the fourth quarter of 2018.

Recent Financial Information

We have not finalized our financial statements for the quarter ended March 31, 2018. Based on our current estimates, as of March 31, 2018, we had approximately $43.5 million in cash, cash equivalents and investments. 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 period ended March 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.

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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	4,500,000 shares
Common stock to be outstanding after this offering	21,170,188 shares
Option to purchase additional shares	We have granted the underwriters an option for a period of 30 days to purchase an additional 675,000 shares of common stock.
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 $37.8 million, or $43.5 million if the underwriters option is exercised in full, based on an assumed public offering price of $9.01 per share, which was the last reported sale price of our common stock on The Nasdaq Global Market on April 16, 2018. We intend to use the net proceeds of this offering for general corporate purposes, which may include funding new and ongoing research and development, capital expenditures, accelerating manufacturing and regulatory activities, initializing commercialization infrastructure and increasing working capital. See Use of Proceeds.
Risk factors	Investing in our common stock involves significant risks. See Risk Factors, beginning on page S-6 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

The number of shares of our common stock to be outstanding immediately after this offering as shown above is based on 16,670,188 shares of common stock outstanding as of December 31, 2017 and excludes:

- 2,361,360 shares of common stock issuable upon exercise of outstanding options as of December 31, 2017, with a weighted-average exercise price of $5.21 per share;
- 830,600 shares of common stock issuable upon exercise of outstanding options granted after December 31, 2017, with a weighted-average exercise price of $6.50 per share;

299,407 shares of common stock reserved for future issuance under our 2016 Equity Incentive Plan as of December 31, 2017;

106,765 shares of common stock reserved for future issuance under our 2016 Employee Stock Purchase Plan as of December 31, 2017;

1,100,000 shares of common stock reserved for future issuance under our 2018 Equity Inducement Plan following December 31, 2017; and

666,807 additional shares of common stock reserved for future issuance under our 2016 Equity Incentive Plan pursuant to the automatic annual increase in the number of shares reserved under the plan of 4% of the total shares outstanding that took place on January 1, 2018.

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.

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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 I, Item 1A, Risk Factors, in our Annual Report on Form 10-K for the year ended December 31, 2017, which is incorporated herein by reference except as updated below, 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. 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 December 31, 2017, 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. 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.

For example, we may raise money through additional public or private offerings of our equity securities or equity-linked securities, through our sales agreement with JonesTrading Institutional Services LLC, or JonesTrading, pursuant to which we may offer and sell, from time to time through JonesTrading shares of our common stock with aggregate proceeds of up to $20.0 million. Any sales of our equity or equity-linked securities could have a material adverse effect on the market price of our common stock.

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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.

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

We have initiated clinical trials of our lead product candidate pegzilarginase, and the risk of failure for all of our product candidates is high. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete nonclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans for the respective target indications. Clinical testing is expensive, difficult to design and implement and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Further, the results of nonclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials that will likely differ in design and size from early-stage clinical trials, and interim results of a clinical trial do not necessarily predict final results. For example, while we have observed a reduction in blood arginine and arginine metabolite levels due to pegzilarginase in patients with Arginase 1 Deficiency, and a reduction in blood arginine levels due to pegzilarginase in patients with advanced solid tumors and the hematological malignancies AML and MDS, this data may not necessarily be predictive of the final results of all patients intended to be enrolled in these ongoing clinical trials or in future trials, and may also not be predictive of pegzilarginase s ability to reduce arginine or arginine metabolite levels for these patients over a longer term. In addition, our observations of clinically relevant treatment effects in the first two patients in the Phase 1/2 open-label study of pegzilarginase in patients with Arginase 1 Deficiency after eight weeks of dosing may not be representative of our observations with subsequently dosed patients out to eight weeks or longer. Moreover, we have not discussed with FDA the design of a pivotal trial of pegzilarginase for the treatment of Arginase 1 Deficiency, including the endpoints for such a study and the magnitude of treatment effect we would need to demonstrate. Furthermore, our ongoing Phase 1/2 clinical trial for the treatment of patients with Arginase 1 Deficiency and our Phase 1 clinical trials for the treatment of advanced solid tumors will primarily evaluate the safety of our product candidates, and we will not be evaluating the efficacy of our product candidates in these early trials in a formal manner. Moreover, nonclinical and clinical data are often susceptible to

varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in nonclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval.

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

- delay or failure in reaching agreement with the FDA, EMA, MHRA or a comparable foreign regulatory authority on a trial design that we are able to execute;
- delay or failure in obtaining authorization to commence a trial or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a clinical trial;
- delays in reaching, or failure to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with planned trial sites;
- modifications to our ongoing and planned clinical trial protocols due to regulatory requirements or decisions made by regulatory authorities;
- reports of safety issues, side effects or dose-limiting toxicities, or any additional or more severe safety issues in addition to those observed to date;
- inability, delay, or failure in identifying and maintaining a sufficient number of trial sites, many of which may already be engaged in other clinical programs;
- delay or failure in recruiting and enrolling suitable subjects to participate in one or more clinical trials;
- delay or failure in having subjects complete a trial or return for post-treatment follow-up. For instance, in March 2018, a pediatric patient previously dosed in Part 1 of our Phase 1/2 clinical trial of pegzilarginase for the treatment of Arginase 1 Deficiency withdrew from the trial due to personal reasons;
- clinical sites and investigators deviating from the trial protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial;

a clinical hold for any of our ongoing or planned clinical trials, including for pegzilarginase, where a clinical hold in a trial in one indication could result in a clinical hold for clinical trials in other indications;

clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct more clinical trials than we anticipate or abandon product development programs; for example, the FDA may determine that dose findings are inadequate based on results from our Phase 1/2 trial or any future Phase 3 trial in pegzilarginase for the treatment of hyperargininemia secondary to Arginase 1 Deficiency and require additional dose finding studies to inform instructions for use that provide a safe dosing algorithm for pediatric patients;

the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or insufficient or participants may drop out of these clinical trials at a higher rate than we anticipate;

we may experience delays or difficulties in the enrollment of patients with Arginase 1 Deficiency or patients with tumors, including the identification of patients with Arginase 1 Deficiency or development or identification of a test, if needed, to screen for those cancer patients;

our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;

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- we may have difficulty partnering with experienced CROs that can screen for patients with tumors dependent on arginine that pegzilarginase is designed to target and with CROs that can run our clinical trials effectively;

- regulators may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;

- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; or

- there may be changes in governmental regulations or administrative actions.

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

- be delayed in obtaining marketing approval for our product candidates;

- not obtain marketing approval at all;

- cease development of our product candidates;

- obtain approval for indications or patient populations that are not as broad as intended or desired;

- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings that would reduce the potential market for our product candidates or inhibit our ability to successfully commercialize our product candidates;

- be subject to additional post-marketing restrictions and/or testing requirements; or

- have the product removed from the market after obtaining marketing approval.

We do not know whether any of our planned or current nonclinical studies, or ongoing or planned clinical trials, will need to be restructured or will be completed on schedule, or at all. For example, we have previously delayed enrollment of pediatric patients in our Phase 1/2 trial of pegzilarginase for the treatment of Arginase 1 Deficiency due to a difference in opinion with the FDA on data required to support inclusion of pediatric patients. Although we have since reached an agreement with the FDA, the FDA may require additional information or studies to be conducted, or

impose conditions that could further delay or restrict our other planned clinical activities in the future. For example, we are currently administering a large battery of neurocognitive evaluations in pediatric patients in this Phase 1/2 clinical trial, but the FDA may not agree with the overall burden or relevance of including these measures in a Phase 3 trial. In addition, we intend to study surrogate endpoints, such as reduction in blood arginine levels, as the primary endpoints in our Phase 3 clinical trial; however, we may need to show some evidence of stabilization or improvement of clinical signs and symptoms of Arginase 1 Deficiency, such as on neurocognitive outcomes and quality-of-life measurements, to support the primary endpoint. We may face difficulties or delays in enrolling any Phase 3 trial in Arginase 1 Deficiency if we restrict enrollment to patients with baseline clinical abnormalities at a level that provides an opportunity to demonstrate neuromotor and/or neurocognitive outcomes. If we are unable to demonstrate consistent trends on such clinical endpoints, FDA may determine that there is inadequate justification to support that the surrogate endpoint is reasonably likely to predict clinical benefit, which would prohibit approval under the accelerated approval pathway. Significant nonclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may materially harm our business and results of operations.

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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, clinical and commercial collaboration with third-parties, 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, 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 I, Item 1A Risk Factors in our Annual Report on Form 10-K for the year ended December 31, 2017, 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 $37.8 million, or $43.5 million if the underwriters option to purchase additional shares is exercised in full, based on an assumed public offering price of $9.01 per share, which was the last reported sale price of our common stock on The Nasdaq Global Market on April 16, 2018.

We intend to use the net proceeds of this offering for general corporate purposes, which may include funding new and ongoing research and development, capital expenditures, accelerating manufacturing and regulatory activities, initializing commercialization infrastructure and increasing working capital.

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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PRICE RANGE OF COMMON STOCK

Our common stock has been quoted on The Nasdaq Global Market under the symbol AGLE since our initial public offering in April 2016. The following table sets forth, for the periods indicated, the reported high and low sales prices per share of our common stock as reported by The Nasdaq Global Market:

	High	Low
Fiscal Year ended December 31, 2016		
Second Fiscal Quarter (1)	$ 12.75	$ 4.10
Third Fiscal Quarter	$ 8.30	$ 3.89
Fourth Fiscal Quarter	$ 10.34	$ 4.27
Fiscal Year ended December 31, 2017		
First Fiscal Quarter	$ 8.14	$ 3.66
Second Fiscal Quarter	$ 7.74	$ 3.28
Third Fiscal Quarter	$ 5.12	$ 2.81
Fourth Fiscal Quarter	$ 6.24	$ 3.75
Fiscal Year ending December 31, 2018		
First Fiscal Quarter	$ 11.35	$ 4.95
Second Fiscal Quarter (through April 16, 2018)	$ 10.73	$ 7.83

(1) The period reported for the second fiscal quarter is from April 7, 2016 through June 30, 2016.

The last reported sale price for our common stock on April 16, 2018 was $9.01 per share.

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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 December 31, 2017 was approximately $50.3 million, or $3.02 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 December 31, 2017. 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 at the public offering price of $ per share and after deducting underwriting discounts and commissions and estimated offering expenses, our as adjusted net tangible book value as of December 31, 2017 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 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 December 31, 2017	$ 3.02	
Increase in net tangible book value per share attributable to investors purchasing our common stock 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 the underwriters exercises 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 16,670,188 shares of common stock outstanding as of December 31, 2017 and excludes:

- 2,361,360 shares of common stock issuable upon exercise of outstanding options as of December 31, 2017, with a weighted-average exercise price of $5.21 per share;

- 830,600 shares of common stock issuable upon exercise of outstanding options granted after December 31, 2017, with a weighted-average exercise price of $6.50 per share;

299,407 shares of common stock reserved for future issuance under our 2016 Equity Incentive Plan as of December 31, 2017;

106,765 shares of common stock reserved for future issuance under our 2016 Employee Stock Purchase Plan as of December 31, 2017;

1,100,000 shares of common stock reserved for future issuance under our 2018 Equity Inducement Plan following December 31, 2017; and

666,807 additional shares of common stock reserved for future issuance under our 2016 Equity Incentive Plan pursuant to the automatic annual increase in the number of shares reserved under the plan of 4% of the total shares outstanding that took place on January 1, 2018.

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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MATERIAL UNITED STATES FEDERAL INCOME TAX CONSEQUENCES

FOR NON-U.S. HOLDERS OF OUR COMMON STOCK

The following summary describes the material U.S. federal income tax consequences of the acquisition, ownership and disposition of our common stock acquired in this offering by Non-U.S. Holders (as defined below). 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 Non-U.S. Holders 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;
- persons that own, or are deemed to own, more than 5% of our capital stock;
- 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 integrated investment or other risk reduction strategy;
- 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 Non-U.S. Holders 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.

PERSONS CONSIDERING THE PURCHASE OF OUR COMMON STOCK 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 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.

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For the purposes of this discussion, a Non-U.S. Holder is, for U.S. federal income tax purposes, a beneficial owner of common stock that is not a U.S. Holder or a partnership for U.S. federal income tax purposes. A U.S. Holder means a beneficial owner of our common stock 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.

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.

Distributions

We do not expect to make any distributions on our common stock in the foreseeable future. If we do make distributions on our common stock, however, such distributions made to a Non-U.S. Holder of our common stock 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. Any remaining excess will be treated as gain realized on the sale or exchange of our common stock as described below under the section titled Gain on Disposition of Our Common Stock.

Any distribution on our common stock 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 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 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 is held through a financial institution or other agent, to the applicable withholding agent). In general,

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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.

Gain on Disposition of Our Common Stock

Subject to the discussion below under the sections titled Backup Withholding and Information Reporting and Foreign Accounts, 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 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 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, 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 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 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.

See the section titled Foreign Accounts for additional information regarding withholding rules that may apply to proceeds of a disposition of our common stock paid to foreign financial institutions or non-financial foreign entities.

U.S. Federal Estate Tax

The estates of nonresident alien individuals generally are subject to U.S. federal estate tax on property with a U.S. situs. Because we are a U.S. corporation, our common stock will be U.S. situs property and, therefore, will be included in the taxable estate of a nonresident alien decedent, unless an applicable estate tax treaty between the United States and the decedent s country of residence provides otherwise. 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.

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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 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 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.

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 and, on or after January 1, 2019, the gross proceeds of a disposition of our common stock, made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends on, or, on or after January 1, 2019, gross proceeds from the sale or other disposition of, our common stock 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.

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

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EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK, 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

Under the terms and subject to the conditions contained in an underwriting agreement dated April , 2018, we have agreed to sell to the underwriters named below, for whom Evercore Group L.L.C. and BMO Capital Markets Corp. are acting as representatives, the following respective numbers of shares of common stock:

Underwriter	Number of Shares
Evercore Group L.L.C.	
BMO Capital Markets Corp.	
JonesTrading Institutional Services LLC	
Total	

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters are obligated to purchase all the shares of common stock in the offering if any are purchased, other than those shares covered by the option to purchase additional shares described below. The underwriting agreement also provides that, if an underwriter defaults, the purchase commitments of non-defaulting underwriters may be increased or the offering may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

We have granted to the underwriters an option to purchase up to additional shares of common stock at the public offering price, less the underwriting discount. This option is exercisable for a period of 30 days. To the extent that the underwriters exercise this option, the underwriters will purchase additional shares from us in approximately the same proportion as shown in the table above.

The underwriters propose to offer the shares of common stock initially at the public offering price on the cover page of this prospectus supplement and to selling group members at that price less a selling concession of up to $ per share. After the initial offering to the public, the underwriters may change the public offering price and concession and discount to broker/dealers.

The following table shows the public offering price, underwriting discount and proceeds, before expenses, to us. These amounts are shown assuming both no exercise and full exercise of the underwriters option to purchase additional shares.

	Per Share		Total	
	Without Exercise	With Full Exercise	Without Exercise	With Full Exercise
Public offering price of common stock	$	$	$	$
Underwriting discounts and commissions	$	$	$	$
Proceeds, before expenses, to us	$	$	$	$

We have also agreed to reimburse the underwriters for up to $20,000 for their FINRA counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

We estimate that the total expenses of the offering payable by us, excluding underwriting discount, will be approximately $280,000. In addition, Needham & Company, LLC is serving as our independent financial advisor in connection with this offering, for which we will pay an advisory fee of $250,000. The underwriters have agreed to reimburse us for $250,000 of expenses incurred in connection with this offering.

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Pursuant to certain lock-up agreements, we and our executive officers and directors have agreed, subject to certain exceptions, not to, directly or indirectly, (i) offer, sell, assign, transfer, pledge, contract to sell or otherwise dispose of any shares of our common stock (including, without limitation, common stock which may be deemed to be beneficially owned by the party to the lock-up agreement in accordance with the rules and regulations promulgated under the Securities Act (such shares, beneficially owned shares)) or securities convertible into or exercisable or exchangeable for our common stock, (ii) enter into any swap, hedge or similar agreement or arrangement that transfers in whole or in part, the economic risk of ownership of beneficially owned shares or securities convertible into or exercisable or exchangeable for our common stock, whether now owned or hereafter acquired by the party to the lock-up agreement or with respect to which the party to the lock-up agreement has or hereafter acquires the power of disposition, (iii) engage in any short selling of the common stock or securities convertible into or exercisable or exchangeable for our common stock or, (iv) publicly announce the intention to engage in any action described under (i), (ii) or (iii), without the prior written consent of the representatives for a period of 90 days, commencing on, and including, the date of the underwriting agreement and ending on the 90th day following the date of the underwriting agreement.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition. The exceptions permit our executive officers and directors, as parties to the lock-up agreements, among other things and subject to restrictions, to: (a) make certain gifts; (b) make transfers by will or intestate succession; (c) if the party is 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 stockholders, partners, members of, or owners of similar equity interests in the party, or to an affiliate of the party, if such transfer is not for value; (d) if the party is 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 made in connection with the sale or transfer of all of the party s capital stock, partnership interests, membership interests or other similar equity interests, as the case may be, or all or substantially all of the party s assets, in any such case not undertaken for the purpose of avoiding the restrictions imposed by the lock-up agreement; (e) if the party holds our securities in a trust, make transfers to the settlor or beneficiary of such trust or to the estate of a beneficiary of such trust if such transfer is not for value; (f) enter into transactions relating to shares of common stock acquired by the party in the offering or shares of common stock or other securities convertible into or exchangeable for common stock acquired in open market transactions after completion of the offering, provided that no filing under Section 16(a) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, shall be required or shall be voluntarily made in connection with such transactions; (g) make transfers to us pursuant to agreements under which we have the option to repurchase such common stock or a right of first refusal with respect to transfers of such shares upon termination of service of such party; (h) enter into a 10b5-1 trading plan, provided that such plan does not permit the sale of any common stock during the 90-day lock-up period and no public announcement or filing is made regarding such plan during the 90-day lockup period; (i) the sale of common stock or securities convertible into or exchangeable or exercisable for common stock pursuant to a 10b5-1 trading plan in existence and disclosed to the representatives prior to the execution of the underwriting agreement, providing for the sale of common stock by the party, which trading plan meets the requirements of Rule 10b5-1(c) under the Exchange Act; (j) make transfers to us to satisfy tax withholding obligations pursuant to our equity incentive plans disclosed in this prospectus; (k) make transfers pursuant to a bona-fide third-party tender offer, merger, consolidation, binding share exchange or other similar transaction made to all holders of our securities involving a change of control of us, provided that in the event such tender offer, merger, consolidation or other transaction is not completed, such securities held by a party will remain subject to the lock-up agreement; (l) 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; (m) exercise any option, warrant or other right to acquire our common stock, settlement of any stock-settled appreciation rights, restricted stock or restricted stock units,

including through net or cashless exercise, granted and outstanding as of the execution date of the lock-up agreement for such party or upon the completion of the offering; and (n) sell or transfer our securities after the date that is 60 days after the date of the underwriting

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agreement; provided that the number of securities that may be sold or transferred by all of our directors and executive officers (excluding shares sold pursuant to a 10b5-1 trading plan), in aggregate, pursuant to clause (n) may not exceed an aggregate of 1% of the total issued and outstanding shares of our common stock immediately after the closing of this offering, and provided further that, in the case of clauses (a) through (e), (k) and (l) above, the transferee agrees to be bound in writing by the lock-up restrictions.

The exceptions to the lock-up provision also permit us, among other things and subject to restrictions, to: (a) issue common stock and options to purchase common stock, shares of common stock underlying options granted and other securities, each pursuant to any director or employee stock option plan, stock ownership plan or dividend reinvestment plan we may have in effect on the date of the underwriting agreement and described in this prospectus or the registration statement of which this prospectus forms a part; (b) issue common stock pursuant to the conversion of securities that are outstanding on the date of the underwriting agreement and described in this prospectus or the registration statement of which this prospectus forms a part; (c) enter into agreements providing for the issuance by us of shares of common stock or securities convertible into or exchangeable for shares of common stock in connection with the acquisition by us of the securities, business, property or other assets of another person or entity pursuant to an employee benefit plan assumed by us in connection with such acquisition, and issue any such securities pursuant to any such agreement; (d) enter into agreements providing for the issuance of shares of our common stock in connection with joint ventures, commercial relationships or other strategic transactions, and issue any such securities pursuant to any such agreements, provided that the aggregate number of shares of common stock that we may sell or issue or agree to sell or issue pursuant to clauses (c) and (d) above, taken together, do not exceed 5% of the total number of shares of common stock issued and outstanding immediately subsequent to the completion of this offering, and provided further that as a condition to the sale, issuance or transfer of shares of any such securities, the transferee will execute and deliver a lock-up agreement to the representatives; and (e) adopt a new equity incentive plan, file 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 issue securities pursuant to such new equity incentive plan or any other employee benefit or equity plan described in this prospectus or the documents incorporated by reference herein (including, without limitation, the issuance of shares of common stock upon the exercise of options or other securities issued pursuant to such new equity incentive plan).

The shares are listed on The Nasdaq Global Market under the symbol AGLE .

In connection with the offering the underwriters may engage in stabilizing transactions, over-allotment transactions, syndicate covering transactions, penalty bids and passive market making in accordance with Regulation M under the Exchange Act.

Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum.

Over-allotment involves sales by the underwriters of shares in excess of the number of shares the underwriters are obligated to purchase, which creates a syndicate short position. The short position may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by the underwriters is not greater than the number of shares that they may purchase in the over-allotment option. In a naked short position, the number of shares involved is greater than the number of shares in the over-allotment option. The underwriters may close out any covered short position by either exercising their option to purchase additional shares and/or purchasing shares in the open market.

Syndicate covering transactions involve purchases of the common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares. If the underwriters sell more shares than could be covered by the option to purchase additional shares, a naked short position, the position can only be

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closed out by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there could be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.

Penalty bids permit the representatives to reclaim a selling concession from a syndicate member when the common stock originally sold by the syndicate member is purchased in a stabilizing or syndicate covering transaction to cover syndicate short positions.

In passive market making, market makers in the common stock who are underwriters or prospective underwriters may, subject to limitations, make bids for or purchases of our common stock until the time, if any, at which a stabilizing bid is made.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of the common stock. As a result the price of our common stock may be higher than the price that might otherwise exist in the open market. These transactions may be effected on The Nasdaq Global Market or otherwise. The underwriters make no representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

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

Conflicts of Interest

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

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

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NOTICE TO INVESTORS

Notice to prospective investors in the European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), each underwriter represents and agrees that with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, it has not made and will not make an offer of shares which are the subject of the offering contemplated by this prospectus 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 for any such offer; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

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

Notice to prospective investors in the United Kingdom

Each of the underwriters severally represents, warrants and agrees as follows:

(a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000 (FSMA) received by it in connection with the issue or sale of the shares in circumstances in which Section 21 of the FSMA does not apply to us; and

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

Notice to prospective investors in Switzerland

This document is not intended to constitute an offer or solicitation to purchase or invest in the shares described herein. The shares may not be publicly offered, sold or advertised, directly or indirectly, in, into or from Switzerland and will not be listed on the SIX Swiss Exchange or on any other exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares constitutes a prospectus as such term is understood pursuant to article 652a or article 1156 of the Swiss Code of Obligations or a listing prospectus within the meaning of the listing rules of the SIX Swiss Exchange or any other regulated trading facility in Switzerland, and neither this document nor any other offering or marketing material relating to the shares 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, nor the Company nor the shares have been or will be filed with or approved by any Swiss regulatory authority. The

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shares are not subject to the supervision by any Swiss regulatory authority, e.g., the Swiss Financial Markets Supervisory Authority (FINMA), and investors in the shares will not benefit from protection or supervision by such authority.

Notice to prospective investors in Israel

In the State of Israel this prospectus shall not be regarded as an offer to the public to purchase shares of common stock under the Israeli Securities Law, 5728 1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728 1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the Addressed Investors); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728 1968, subject to certain conditions (the Qualified Investors). The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. The company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728 1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for our common stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728 1968. In particular, we may request, as a condition to be offered common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728 1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728 1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728 1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock; (iv) that the shares of common stock that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728 1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728 1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor s name, address and passport number or Israeli identification number.

We have not authorized and do not authorize the making of any offer of securities through any financial intermediary on our behalf, other than offers made by the underwriters and their respective affiliates, with a view to the final placement of the securities as contemplated in this document.

Accordingly, no purchaser of the shares, other than the underwriters, is authorized to make any further offer of shares on our behalf or on behalf of the underwriters

Notice to prospective investors in 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 the shares of common stock may not be circulated or distributed, nor may the shares of common stock 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, or 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.

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Where the shares of common stock 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) the sole purpose of which 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 common stock pursuant to an offer made under Section 275 of the SFA except:

(a) 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;

(b) where no consideration is or will be given for the transfer;

(c) where the transfer is by operation of law;

(d) as specified in Section 276(7) of the SFA; or

(e) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Notice to prospective investors in Canada

Resale Restrictions

The distribution of common stock in Canada is being made only in the provinces of Ontario, Quebec, Alberta and British Columbia on a private placement basis exempt from the requirement that we prepare and file a prospectus with the securities regulatory authorities in each province where trades of these securities are made. Any resale of the common stock in Canada must be made under applicable securities laws which may vary depending on the relevant jurisdiction, and which may require resales to be made under available statutory exemptions or under a discretionary exemption granted by the applicable Canadian securities regulatory authority. Purchasers are advised to seek legal advice prior to any resale of the securities.

Representations of Canadian Purchasers

By purchasing common stock in Canada and accepting delivery of a purchase confirmation, a purchaser is representing to us and the dealer from whom the purchase confirmation is received that:

the purchaser is entitled under applicable provincial securities laws to purchase the shares of common stock without the benefit of a prospectus qualified under those securities laws as it is an accredited investor as defined under National Instrument 45-106 *Prospectus Exemptions*,

the purchaser is a permitted client as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*,

where required by law, the purchaser is purchasing as principal and not as agent, and

the purchaser has reviewed the text above under Resale Restrictions.

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Conflicts of Interest

Canadian purchasers are hereby notified that underwriters are relying on the exemption set out in section 3A.3 or 3A.4, if applicable, of National Instrument 33-105 *Underwriting Conflicts* from having to provide certain conflict of interest disclosure in this document.

Statutory Rights of Action

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if the offering memorandum (including any amendment thereto) such as this document 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 of these securities in Canada 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.

Enforcement of Legal Rights

All of our directors and officers as well as the experts named herein may be located outside of Canada and, as a result, it may not be possible for Canadian purchasers to effect service of process within Canada upon us or those persons. All or a substantial portion of our assets and the assets of those persons may be located outside of Canada and, as a result, it may not be possible to satisfy a judgment against us or those persons in Canada or to enforce a judgment obtained in Canadian courts against us or those persons outside of Canada.

Taxation and Eligibility for Investment

Canadian purchasers of our common stock should consult their own legal and tax advisors with respect to the tax consequences of an investment in the shares of common stock in their particular circumstances and about the eligibility of the shares of common stock for investment by the purchaser under relevant Canadian legislation.

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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 shares of common stock 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 common stock 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. 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 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 Current Reports on Form 8-K filed on March 26, 2018, and April 16, 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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4,500,000 Shares

Common Stock

PROSPECTUS SUPPLEMENT