
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549**

**FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

Aeglea BioTherapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

46-4312787
(I.R.S. Employer
Identification No.)

**901 S. MoPac Expressway
Barton Oaks Plaza One
Suite 250
Austin, TX 78746
(512) 942-2935**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Anthony G. Quinn, M.B Ch.B, Ph.D.
Chief Executive Officer
Aeglea BioTherapeutics, Inc.
901 S. MoPac Expressway
Barton Oaks Plaza One
Suite 250
Austin, TX 78746
(512) 942-2935

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Robert A. Freedman, Esq.
Effie Toshav, Esq.
Fenwick & West LLP
801 California Street
Mountain View, California 94041
(650) 988-8500

Charles N. York II
Chief Financial Officer
Aeglea BioTherapeutics, Inc.
901 S. MoPac Expressway
Barton Oaks Plaza One
Suite 250
Austin, TX 78746
(512) 942-2935

Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this Registration Statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box:

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box:

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following

box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering:

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earliest effective registration statement for the same offering:

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I. D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of “large accelerated filer,” “accelerated filer,” “smaller reporting company,” and “emerging growth company” in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer Accelerated filer
 Non-accelerated filer Smaller reporting company
 Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered (1)	Amount to be Registered (1)(2)	Proposed Maximum Offering Price Per Security (3)	Proposed Maximum Aggregate Offering Price (3)	Amount of Registration Fee (4)
Common stock, \$0.0001 par value per share				
Preferred stock, \$0.0001 par value per share				
Debt securities				
Warrants				
Subscription rights				
Units				
Total			\$275,000,000	\$33,330

- (1) There is being registered hereunder an indeterminate number of shares of (a) common stock, (b) preferred stock, (c) debt securities, (d) warrants to purchase common stock, preferred stock or debt securities of the Registrant, (e) subscription rights to purchase common stock, preferred stock or debt securities of the Registrant, and (f) units, consisting of some or all of these securities in any combination, as may be sold from time to time by the Registrant. Any securities registered hereunder may be sold separately or as units with other securities registered hereunder. There are also being registered hereunder an indeterminate number of shares of common stock, preferred stock and debt securities as shall be issuable upon conversion, exchange or exercise of any securities that provide for such issuance. In no event will the aggregate offering price of all types of securities issued by the Registrant pursuant to this registration statement exceed \$275,000,000.
- (2) Pursuant to Rule 416(a), this registration statement also covers any additional securities that may be offered or issued in connection with any stock split, stock dividend or similar transaction.
- (3) The proposed maximum offering price per share and proposed maximum aggregate offering price for each type of security will be determined from time to time by the Registrant in connection with the issuance by the Registrant of the securities registered hereunder.
- (4) Calculated pursuant to Rule 457(o) under the Securities Act of 1933, as amended. Pursuant to Rule 415(a)(6) under the Securities Act, the Registrant hereby offsets the total registration fee due under this Registration Statement by the amount of the filing fee associated with the unsold securities from the Registrant’s Form S-3 Registration Statement, filed with the Securities and Exchange Commission, or the SEC, on May 1, 2017 (SEC File No. 333-217573), as amended on May 23, 2017 and declared effective by the SEC on May 30, 2017 (the “Prior Registration Statement”), which included \$150,000,000 of shares of (a) common stock, (b) preferred stock, (c) debt securities, (d) warrants to purchase common stock, preferred stock or debt securities of the Registrant, (e) subscription rights to purchase common stock, preferred stock or debt securities of the Registrant, and (f) units, consisting of some or all of these securities in any combination, as may be sold from time to time by the Registrant, or collectively, the Shelf Securities, of which \$80,327,920 of the Shelf Securities remain unsold as the date of filing of this Registration Statement. The Registrant has determined to include in this Registration Statement the unsold Shelf Securities under the Prior Registration Statement having an aggregate offering price of \$80,327,920, or the Unsold Securities. The associated filing fee of \$9,735 for the Unsold Securities under the Prior Registration Statement is hereby used to partially offset the current registration fee due, resulting in an additional registration fee of \$23,595 due in connection with the filing of this Registration Statement, which has been paid in connection with the filing of this Registration Statement. To the extent that, after the filing date hereof and prior to the effectiveness of this Registration Statement, the Registrant sells any Unsold Securities pursuant to the Prior Registration Statement, the Registrant will identify in a pre-effective amendment to this Registration Statement the updated amount of Unsold Securities from the Prior Registration Statement to be included in this Registration Statement pursuant to Rule 415(a)(6) under the Securities Act and the updated amount of securities to be registered on this Registration Statement. Pursuant to Rule 415(a)(6) under the Securities Act, the offering of the Unsold Securities under the Prior Registration Statement will be deemed terminated as of the date of effectiveness of this Registration Statement

The Registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

EXPLANATORY NOTE

This registration statement contains two prospectuses:

- a base prospectus, which covers the offering, issuance and sale by us of up to a maximum aggregate offering price of \$275,000,000 of our common stock, 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; and
- a sales agreement prospectus supplement covering the offering, issuance and sale by us of up to a maximum aggregate offering price of \$60,000,000 of our common stock that may be issued and sold under an Open Market Sale AgreementSM dated December 21, 2018 with Jefferies LLC.

The base prospectus immediately follows this explanatory note. The specific terms of any securities to be offered pursuant to the base prospectus will be specified in a prospectus supplement to the base prospectus. The sales agreement prospectus supplement immediately follows the base prospectus. The \$60,000,000 of common stock that may be offered, issued and sold under the sales agreement prospectus supplement is included in the \$275,000,000 of securities that may be offered, issued and sold by us under the base prospectus.

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The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities, and it is not soliciting an offer to buy these securities, in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED DECEMBER 21, 2018

PROSPECTUS

\$275,000,000



Aeglea BioTherapeutics, Inc.

Common Stock, Preferred Stock, Debt Securities, Warrants, Subscription Rights and Units

From time to time, we may offer up to \$275,000,000 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 \$275,000,000.

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 December 20, 2018 the last reported sales price for our common stock was \$7.07 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 _____, 2018

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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 \$275,000,000. 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 to Aeglea BioTherapeutics, Inc., a Delaware corporation, and its consolidated subsidiaries.

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

Our drug-hunting capabilities in enzyme engineering, preclinical disease 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 lead product candidate, 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 1 Deficiency, a rare genetic disease, as well as some cancers which have been shown to have a metabolic dependence on arginine. Pegzilarginase is being evaluated in multiple ongoing clinical trials and we expect to start a single, global pivotal Phase 3 trial in patients with Arginase 1 Deficiency in the second quarter of 2019. Currently, our development consists of a Phase 1/2 clinical trial for the treatment of Arginase 1 Deficiency, an open-label extension study for patients with Arginase 1 Deficiency, a Phase 1 clinical trial for the treatment of advanced solid tumors, and a Phase 1/2 combination clinical trial of pegzilarginase with pembrolizumab for the treatment of patients with small cell lung cancer (SCLC). We are also building a pipeline of additional product candidates targeting key amino acids and other metabolites, including AEB4104 for the treatment of homocystinuria, AEB5100 for the treatment of cystinuria, and AEB2109 for the treatment of cancer.

Rare Genetic Diseases

Pegzilarginase in Patients with Arginase 1 Deficiency

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

In December 2018, we announced the design of our single, global pivotal Phase 3 PEACE (Pegzilarginase Effect on Arginase 1 Deficiency Clinical Endpoints) trial with a primary endpoint of plasma arginine reduction and secondary endpoints which include assessments of clinical outcomes, safety and pharmacokinetics. We have aligned the trial design and endpoints with input from the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA). We expect to dose the first patient in the PEACE trial in the second quarter of 2019 and expect that data from the Phase 3 PEACE trial will be available in the first quarter of 2021. Additional interim clinical data from our Phase 1/2 clinical trial reporting repeat dose administration of pegzilarginase is expected in the first half of 2019. Our expectation is that the data from this Phase 3 trial should be sufficient to support marketing applications for pegzilarginase in Arginase 1 Deficiency.

In October 2018, we announced new positive interim clinical data at the 2018 American Society of Human Genetics (ASHG) Conference from our ongoing Phase 1/2 trial of pegzilarginase in patients with Arginase 1 Deficiency. Highlights of the presentation, where we reported clinical improvements with repeat dose administration of pegzilarginase after only 8 weeks, included the following:

- 100% of patients (6 out of 6) who completed Part 2 (repeat dose) of the study achieved consistent levels of reduced arginine, which was also accompanied by marked and sustained decreases in guanidino compounds;
- Comprehensive baseline profiling of patients with Arginase 1 Deficiency demonstrated quantifiable abnormalities in mobility and/or adaptive behavior in 94% of patients (15 out of 16);
- Pegzilarginase was well tolerated; most treatment-related adverse events were mild, and hypersensitivity reactions were manageable with standard measures and all patients continued study treatment;
- 67% of patients (4 out of 6) had clinically meaningful improvements in mobility and/or adaptive behavior after only 8 weeks of repeat dosing with pegzilarginase; and
- Completed and exceeded our enrollment target with 16 patients in the Phase 1/2.

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

AEB4104 in Patients with Homocystinuria

Homocystinuria is an inherited disorder of methionine metabolism caused by mutations in CBS and other genes leading to elevated levels of plasma and tissue homocysteine and homocystine, which affect multiple organ systems and cause early mortality. Current disease management, which includes dietary protein (methionine) restriction, vitamins, and betaine supplementation, is insufficient to effectively control the more severe forms of the disease. Given the severity of the disease, the limitations of current disease management approaches, and the data demonstrating improved survival in a preclinical model of the disease, AEB4104 is being advanced into IND-enabling studies in the first half of 2019.

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

AEB5100 in Patients with Cystinuria

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

In October 2018, we announced preclinical efficacy data on our AEB5100 cystinuria therapeutic program at the 2018 American Society of Nephrology (ASN) Conference, demonstrating that AEB5100 lowered blood levels of cystine and cysteine, decreased the amount of cystine in the urine and reduced kidney stone formation in a preclinical model of cystinuria. Given the compelling preclinical data and the limitations of current disease management approaches, AEB5100 is being advanced into IND-enabling studies and we anticipate beginning GLP manufacturing for toxicology studies in the first half of 2019.

Cancer

Pegzilarginase with Pembrolizumab in Patients with Small Cell Lung Cancer

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

Pegzilarginase in Patients with Advanced Solid Tumors

In October 2018, we presented interim clinical data at the European Society for Medical Oncology (ESMO) 2018 Congress, demonstrating that pegzilarginase monotherapy resulted in anti-tumor activity in heavily pre-treated patients with advanced melanoma. The investigator-assessed responses in 11 cutaneous melanoma patients and 15 uveal melanoma patients revealed that one patient achieved a confirmed partial response (PR) at week 20 and eight patients had stable disease (SD) at week 8 or later. Six patients remained on treatment at the time of the data cutoff. Anti-tumor activity appeared greater in tumors lacking argininosuccinate synthetase 1 (ASS1) expression, which is consistent with preclinical studies that suggest tumors lacking ASS1 expression are dependent on extracellular arginine for survival.

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

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 \$275,000,000. 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.

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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.

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.

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 II, Item 1A, “Risk Factors,” in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2018, which is incorporated herein by reference, and may be amended, supplemented or superseded from time to time by other reports we file with the 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.

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 regarding expectations and intentions, costs and expenses, outcome of contingencies, financial condition, results of operations, liquidity, cost savings, objectives of management, debt financing, our future results of operations and financial position, business strategies, market size, potential growth opportunities, clinical development activities, efficacy and safety profile of our product candidates, our ability to maintain and recognize the benefits of certain designations received by product candidates, timing and results of our nonclinical studies and clinical trials, the receipt and timing of potential regulatory designations, the achievement of clinical and commercial milestones, the advancement of our technologies and our proprietary product candidates, approvals and commercialization of product candidates and other statements that are not historical facts. You can find many of these statements by looking for words like “believes,” “expects,” “anticipates,” “estimates,” “may,” “might,” “should,” “will,” “could,” “plan,” “intend,” “project,” “seek” or similar expressions in this prospectus, in documents incorporated by reference into this prospectus or any free writing prospectus. We intend that such forward-looking statements be subject to the safe harbors created thereby.

These forward-looking statements are based on the current beliefs and expectations of our management and are subject to significant risks and uncertainties. If underlying assumptions prove inaccurate or unknown risks or uncertainties materialize, actual results may differ materially from current expectations and projections. Factors that might cause such a difference include those discussed in Part II, Item 1A, “Risk Factors,” in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2018, as well as those discussed in this prospectus, the documents incorporated by reference into this prospectus 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 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.

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. 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.aeglebio.com>. However, the information on our website is not a part of this prospectus and is not incorporated by reference into this prospectus.

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, 2017, filed with the SEC on March 13, 2018, including certain information incorporated by reference therein from our Definitive Proxy Statement for our 2018 annual meeting of stockholders filed with the SEC on April 16, 2018;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2018, June 30, 2018 and September 30, 2018, filed with the SEC on May 8, 2018, August 9, 2018 and November 8, 2018, respectively;
- our Current Reports on Form 8-K filed on March 26, 2018, April 16, 2018, April 19, 2018, June 8, 2018, July 16, 2018, July 23, 2018, October 10, 2018, November 29, 2018 and December 21, 2018;
- 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.

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.

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.

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.

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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.

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.

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 September 30, 2018, there were 22,098,218 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, 2017, 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, as subsequently amended, certain of our stock holders are entitled to rights with respect to the registration of their shares under the Securities Act until the earliest of (a) April 12, 2021, (b) the date on which such holder ceases to hold registrable securities, or (c) such holder's registrable securities could be sold without any restriction on volume or manner of sale in any three-month period under Rule 144 or any successor rule, 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.

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Expenses of registration rights

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

Expiration of registration rights

The registration rights described above will expire, with respect to any particular holder of these rights, on the earlier of the fifth anniversary of the closing of 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.
- **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.

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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."

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 \$275,000,000 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 \$275,000,000. 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 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.

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.

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.

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, 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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The information in this preliminary prospectus supplement and the accompanying prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus supplement and accompanying prospectus are not an offer to sell these securities and they are not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to completion, dated December 21, 2018

PROSPECTUS SUPPLEMENT



Up to \$60,000,000

Common Stock

We have entered into an Open Market Sale AgreementSM, or sales agreement, with Jefferies LLC, or Jefferies, dated December 21, 2018, relating to the sale of shares of our common stock offered by this prospectus supplement. In accordance with the terms of the sales agreement, under this prospectus supplement we may offer and sell shares of our common stock, \$0.0001 par value per share, having an aggregate offering price of up to \$60,000,000 from time to time through Jefferies, acting as our agent.

Sales of our common stock, if any, under this prospectus supplement will be made by any method permitted that is deemed an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended, or the Securities Act. Jefferies is not required to sell any specific amount, but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Jefferies will be entitled to compensation at a commission rate of 3.0% of the gross sales price per share sold under the sales agreement. See “Plan of Distribution” beginning on page S-14 for additional information regarding the compensation to be paid to Jefferies. In connection with the sale of the common stock on our behalf, Jefferies will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Jefferies with respect to certain liabilities, including liabilities under the Securities Act.

Our common stock is listed on the Nasdaq Global Market under the symbol “AGLE.” On December 20, 2018, the last reported sale price of our common stock on the Nasdaq Global Market was \$7.07 per share.

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE “[RISK FACTORS](#)” ON PAGE S-8 OF THIS PROSPECTUS SUPPLEMENT AND IN THE DOCUMENTS INCORPORATED BY REFERENCE IN THIS PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR COMMON STOCK.

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

Jefferies

The date of this prospectus supplement is _____, 2018.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement is part of a registration statement that we have filed with the Securities and Exchange Commission, or SEC, utilizing a “shelf” registration process, and relates to the offering of our common stock. Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus supplement, the accompanying base prospectus and all of the information incorporated by reference herein and therein, as well as the additional information described under the heading “Where You Can Find More Information; Incorporation by Reference.” These documents contain important information that you should consider when making your investment decision.

We provide information to you about this offering of our common stock in two separate documents that are bound together: (1) this prospectus supplement, which describes the specific details regarding this offering; and (2) the accompanying base prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this “prospectus,” we are referring to both documents combined. If information in this prospectus supplement is inconsistent with the accompanying base prospectus, you should rely on this prospectus supplement. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in any document incorporated by reference in this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. 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 supplement—the statement in the document having the later date modifies or supersedes the earlier statement.

You should rely only on the information contained in or incorporated by reference in this prospectus supplement, the accompanying base prospectus and any free writing prospectus that we may authorize for use in connection with this offering. We have not, and Jefferies has not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and Jefferies is not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should assume that the information appearing in this prospectus supplement, the accompanying base prospectus, the documents incorporated by reference herein and therein and any free writing prospectus that we have authorized for use in connection with this offering, 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. You should read this prospectus supplement, the accompanying base prospectus, the documents incorporated by reference herein and therein and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision.

When we refer to “Aeglea,” “we,” “our,” “us,” the “Registrant,” the “Company” and “our company” in this prospectus supplement, we mean Aeglea BioTherapeutics, Inc., a Delaware corporation, and its subsidiaries taken as a whole, unless otherwise specified.

“Aeglea” and all product candidate names are our common law trademarks. This prospectus supplement also includes trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this prospectus supplement appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

Available Information

We file reports, proxy statements and other information with the SEC. The SEC maintains a web site that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is www.sec.gov.

Our web site address is <http://www.aegleabio.com>. The information on our web site, however, is not, and should not be deemed to be, a part of this prospectus supplement.

This prospectus supplement and the accompanying base prospectus are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement. Statements in this prospectus supplement or the accompanying base prospectus about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement through the SEC's website, as provided above, or at our principal executive offices, 901 S. MoPac Expressway, Barton Oaks Plaza One, Suite 250, Austin, TX 78746, during normal business hours.

Incorporation 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 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. 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:

- Our Annual Report on Form 10-K for the year ended December 31, 2017, filed with the SEC on March 13, 2018, including certain information incorporated by reference therein from our Definitive Proxy Statement for our 2018 annual meeting of stockholders filed with the SEC on April 16, 2018;
- Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2018, June 30, 2018 and September 30, 2018, filed with the SEC on May 8, 2018, August 9, 2018 and November 8, 2018, respectively;
- Our Current Reports on Form 8-K filed on March 26, 2018, April 16, 2018, April 19, 2018, June 8, 2018, July 16, 2018, July 23, 2018, October 10, 2018, November 29, 2018 and December 21, 2018; and
- The description of our Common Stock contained in our Registration Statement on Form 8-A, filed with the SEC on March 28, 2016, and any amendment or report filed with the SEC for the purpose of updating the description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference in this prospectus supplement and deemed to be part of this prospectus supplement from the date of the filing of such reports and documents.

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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 supplement 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.

THE COMPANY

Company Overview

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

Our drug-hunting capabilities in enzyme engineering, preclinical disease 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 lead product candidate, 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 1 Deficiency, a rare genetic disease, as well as some cancers which have been shown to have a metabolic dependence on arginine. Pegzilarginase is being evaluated in multiple ongoing clinical trials and we expect to start a single, global pivotal Phase 3 trial in patients with Arginase 1 Deficiency in the second quarter of 2019. Currently, our development consists of a Phase 1/2 clinical trial for the treatment of Arginase 1 Deficiency, an open-label extension study for patients with Arginase 1 Deficiency, a Phase 1 clinical trial for the treatment of advanced solid tumors, and a Phase 1/2 combination clinical trial of pegzilarginase with pembrolizumab for the treatment of patients with small cell lung cancer (SCLC). We are also building a pipeline of additional product candidates targeting key amino acids and other metabolites, including AEB4104 for the treatment of homocystinuria, AEB5100 for the treatment of cystinuria, and AEB2109 for the treatment of cancer.

Rare Genetic Diseases

Pegzilarginase in Patients with Arginase 1 Deficiency

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

In December 2018, we announced the design of our single, global pivotal Phase 3 PEACE (Pegzilarginase Effect on Arginase 1 Deficiency Clinical Endpoints) trial with a primary endpoint of plasma arginine reduction and secondary endpoints which include assessments of clinical outcomes, safety and pharmacokinetics. We have aligned the trial design and endpoints with input from the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA). We expect to dose the first patient in the PEACE trial in the second quarter of 2019 and expect that data from the Phase 3 PEACE trial will be available in the first quarter of 2021. Additional interim clinical data from our Phase 1/2 clinical trial reporting repeat dose administration of pegzilarginase is expected in the first half of 2019. Our expectation is that the data from this Phase 3 trial should be sufficient to support marketing applications for pegzilarginase in Arginase 1 Deficiency.

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In October 2018, we announced new positive interim clinical data at the 2018 American Society of Human Genetics (ASHG) Conference from our ongoing Phase 1/2 trial of pegzilarginase in patients with Arginase 1 Deficiency. Highlights of the presentation, where we reported clinical improvements with repeat dose administration of pegzilarginase after only 8 weeks, included the following:

- 100% of patients (6 out of 6) who completed Part 2 (repeat dose) of the study achieved consistent levels of reduced arginine, which was also accompanied by marked and sustained decreases in guanidino compounds;
- Comprehensive baseline profiling of patients with Arginase 1 Deficiency demonstrated quantifiable abnormalities in mobility and/or adaptive behavior in 94% of patients (15 out of 16);
- Pegzilarginase was well tolerated; most treatment-related adverse events were mild, and hypersensitivity reactions were manageable with standard measures and all patients continued study treatment;
- 67% of patients (4 out of 6) had clinically meaningful improvements in mobility and/or adaptive behavior after only 8 weeks of repeat dosing with pegzilarginase; and
- Completed and exceeded our enrollment target with 16 patients in the Phase 1/2.

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

AEB4104 in Patients with Homocystinuria

Homocystinuria is an inherited disorder of methionine metabolism caused by mutations in CBS and other genes leading to elevated levels of plasma and tissue homocysteine and homocystine, which affect multiple organ systems and cause early mortality. Current disease management, which includes dietary protein (methionine) restriction, vitamins, and betaine supplementation, is insufficient to effectively control the more severe forms of the disease. Given the severity of the disease, the limitations of current disease management approaches, and the data demonstrating improved survival in a preclinical model of the disease, AEB4104 is being advanced into IND-enabling studies in the first half of 2019.

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

AEB5100 in Patients with Cystinuria

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

In October 2018, we announced preclinical efficacy data on our AEB5100 cystinuria therapeutic program at the 2018 American Society of Nephrology (ASN) Conference, demonstrating that AEB5100 lowered blood

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levels of cystine and cysteine, decreased the amount of cystine in the urine and reduced kidney stone formation in a preclinical model of cystinuria. Given the compelling preclinical data and the limitations of current disease management approaches, AEB5100 is being advanced into IND-enabling studies and we anticipate beginning GLP manufacturing for toxicology studies in the first half of 2019.

Cancer

Pegzilarginase with Pembrolizumab in Patients with Small Cell Lung Cancer

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

Pegzilarginase in Patients with Advanced Solid Tumors

In October 2018, we presented interim clinical data at the European Society for Medical Oncology (ESMO) 2018 Congress, demonstrating that pegzilarginase monotherapy resulted in anti-tumor activity in heavily pre-treated patients with advanced melanoma. The investigator-assessed responses in 11 cutaneous melanoma patients and 15 uveal melanoma patients revealed that one patient achieved a confirmed partial response (PR) at week 20 and eight patients had stable disease (SD) at week 8 or later. Six patients remained on treatment at the time of the data cutoff. Anti-tumor activity appeared greater in tumors lacking argininosuccinate synthetase 1 (ASS1) expression, which is consistent with preclinical studies that suggest tumors lacking ASS1 expression are dependent on extracellular arginine for survival.

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

Recent Developments

In May 2017, we entered into an "at-the-market" program and sales agreement with JonesTrading Institutional Services LLC, under which we may, from time to time, offer and sell common stock having an aggregate offering value of up to \$20.0 million, referred to as our "at-the-market" offering. In October 2018, we sold 1,845,820 shares of our common stock under the at-the-market program for aggregate net proceeds of \$16.4 million. On December 17, 2018, we provided notice to JonesTrading Institutional Services LLC of our decision to terminate the sales agreement and "at-the-market" offering program, effective December 21, 2018.

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

THE OFFERING	
Common stock offered by us	Shares of our common stock having an aggregate offering price of up to \$60,000,000.
Common shares to be outstanding following the offering	Up to 30,584,780 shares (as more fully described in the notes following this table), assuming sales of 8,486,563 shares of our common stock in this offering at an offering price of \$7.07 per share, which was the last reported sale price of our common shares on The Nasdaq Global Market on December 20, 2018. The actual number of shares issued will vary depending on the sales price under this offering.
Manner of offering	“At the market offering” that may be made from time to time on the Nasdaq Global Market or other existing trading market for our common stock through our agent, Jefferies LLC. See the section entitled “Plan of Distribution” on page S-14 of this prospectus supplement.
Use of proceeds	We intend to use the net proceeds of this offering primarily to fund research and development of our product candidates, working capital, capital expenditures and other general corporate purposes. See the section entitled “Use of Proceeds” on page S-11 of this prospectus supplement.
Risk factors	See “Risk Factors” beginning on page S-8 of this prospectus supplement and the other information included in, or incorporated by reference into, this prospectus supplement for a discussion of certain factors you should carefully consider before deciding to invest in shares of our common stock.
Nasdaq Global Market symbol	AGLE

RISK FACTORS

Investment in any securities offered pursuant to this prospectus supplement and the accompanying base prospectus involves risks. You should carefully consider the risk factors described below and in our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2018, incorporated by reference in this prospectus supplement, any amendment or update thereto reflected in subsequent filings with the SEC, including in our Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q, and all other information contained or incorporated by reference in this prospectus supplement, as updated by our subsequent filings under the Exchange Act. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.

Risks Relating to this Offering

If you purchase shares of our common stock sold in this offering, you will experience immediate and substantial dilution in the net tangible book value of your shares. In addition, we may issue additional equity or convertible debt securities in the future, which may result in additional dilution to you.

The price per share of our common stock being offered may be higher than the net tangible book value per share of our outstanding common stock prior to this offering. Assuming that an aggregate of 8,486,563 shares of our common stock are sold at a price of \$7.07 per share, the last reported sale price of our common stock on the Nasdaq Global Market on December 20, 2018, for aggregate gross proceeds of approximately \$60.0 million, and after deducting commissions and estimated offering expenses payable by us, new investors in this offering will incur immediate dilution of \$3.09 per share. For a more detailed discussion of the foregoing, see the section entitled “Dilution” below. To the extent outstanding stock options or warrants are exercised, there will be further dilution to new investors. In addition, to the extent we need to raise additional capital in the future and we issue additional shares of common stock or securities convertible or exchangeable for our common stock, our then existing stockholders may experience dilution and the new securities may have rights senior to those of our common stock offered in this offering.

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

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section entitled “Use of Proceeds,” and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. Our management might not apply our net proceeds in ways that ultimately increase the value of your investment. We expect to use the net proceeds from this offering to fund research and development of our product candidates, working capital, capital expenditures and other general corporate purposes. The failure by our management to apply these funds effectively could harm our business. Pending their use, we plan to invest the net proceeds from this offering in short-term and long-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or guaranteed obligations of the U.S. government. These investments may not yield a favorable return to our stockholders. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

The actual number of shares we will issue under the sales agreement, at any one time or in total, is uncertain.

Subject to certain limitations in the sales agreement and compliance with applicable law, we have the discretion to deliver a placement notice to Jefferies at any time throughout the term of the sales agreement. The number of shares that are sold by Jefferies after delivering a placement notice will fluctuate based on the market price of the common shares during the sales period and limits we set with Jefferies. Because the price per share of each share sold will fluctuate based on the market price of our common stock during the sales period, it is not possible at this stage to predict the number of shares that will be ultimately issued.

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The common stock offered hereby will be sold in “at the market offerings”, and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares sold, and there is no minimum or maximum sales price. Investors may experience a decline in the value of their shares as a result of share sales made at prices lower than the prices they paid.

CAUTIONARY NOTE REGARDING 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 regarding expectations and intentions, costs and expenses, outcome of contingencies, financial condition, results of operations, liquidity, cost savings, objectives of management, debt financing, our future results of operations and financial position, business strategies, market size, potential growth opportunities, clinical development activities, efficacy and safety profile of our product candidates, our ability to maintain and recognize the benefits of certain designations received by product candidates, timing and results of our nonclinical studies and clinical trials, the receipt and timing of potential regulatory designations, the achievement of clinical and commercial milestones, the advancement of our technologies and our proprietary product candidates, approvals and commercialization of product candidates and other statements that are not historical facts. You can find many of these statements by looking for words like “believes,” “expects,” “anticipates,” “estimates,” “may,” “might,” “should,” “will,” “could,” “plan,” “intend,” “project,” “seek” or similar expressions in this prospectus, the documents incorporated by reference into this prospectus and any free writing prospectus. We intend that such forward-looking statements be subject to the safe harbors created thereby.

These forward-looking statements are based on the current beliefs and expectations of our management and are subject to significant risks and uncertainties. If underlying assumptions prove inaccurate or unknown risks or uncertainties materialize, actual results may differ materially from current expectations and projections. Factors that might cause such a difference include those discussed in Part II, Item 1A, “Risk Factors,” in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2018, as well as those discussed in this prospectus, the documents incorporated by reference into this prospectus 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 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.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$60,000,000 time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time.

We currently intend to use any net proceeds from the sale of securities under this prospectus primarily to fund research and development of our product candidates, working capital, capital expenditures and other general corporate purposes. Additionally, we may use a portion of the net proceeds from this offering to expand our current business by in-licensing or acquiring, as the case may be, commercial products, product candidates, technologies, compounds, other assets or complementary businesses, using cash or shares of our common stock. However, we have no current commitments or obligations to do so.

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, the accompanying base prospectus and the documents incorporated by reference herein and therein, as well as the amount of cash used in our operations. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the uses described above, we plan to invest the net proceeds from this offering in short-term or long-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or guaranteed obligations of the U.S. government.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, business prospects and other factors the board of directors deems relevant, and subject to the restrictions contained in any future financing instruments.

DILUTION

If you invest in our common stock, your interest will be diluted to the extent of the difference between the price per share you pay in this offering and the net tangible book value per share of our common stock immediately after this offering. Our net tangible book value of our common stock as of September 30, 2018 was approximately \$63.7 million, or approximately \$2.88 per share of common stock based upon 22,098,218 shares outstanding. Net tangible book value per share is equal to our total tangible assets, less our total liabilities, divided by the total number of shares outstanding as of September 30, 2018.

After giving effect to the sale of our common stock in the aggregate amount of \$60.0 million at an assumed offering price of \$7.07 per share, the last reported sale price of our common stock on the Nasdaq Global Market on December 20, 2018, and after deducting commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2018 would have been \$63.7 million, or \$2.88 per share of common stock. This represents an immediate increase in net tangible book value of \$1.09 per share to our existing stockholders and an immediate dilution in net tangible book value of \$3.09 per share to new investors in this offering.

The following table illustrates this calculation on a per share basis. The as adjusted information is illustrative only and will adjust based on the actual price to the public, the actual number of shares sold and other terms of the offering determined at the time shares of our common stock are sold pursuant to this prospectus supplement. The as adjusted information assumes that all of our common stock in the aggregate amount of \$60.0 million is sold at the assumed offering price of \$7.07 per share, the last reported sale price of our common stock on the Nasdaq Global Market on December 20, 2018. The shares sold in this offering, if any, will be sold from time to time at various prices.

Assumed public offering price per share	\$7.07
Net tangible book value per share as of September 30, 2018	\$2.88
Increase in net tangible book value per share attributable to the offering	<u>1.09</u>
As adjusted net tangible book value per share after giving effect to the offering	<u>3.98</u>
Dilution per share to new investors participating in the offering	<u>\$3.09</u>

The number of shares of our common stock to be outstanding immediately after this offering is based on 22,098,218 shares of our common stock outstanding as of September 30, 2018. The number of shares outstanding as of September 30, 2018 excludes:

- 3,031,347 shares of common stock issuable upon exercise of options outstanding as of September 30, 2018, with a weighted average exercise price of \$6.16 per share;
- 1,121,472 shares of common stock reserved and available for future issuance as of September 30, 2018, under our equity incentives plans, consisting of (1) 84,521 shares of common stock reserved and available for issuance under our 2016 Equity Incentive Plan as of September 30, 2018, (2) 50,851 shares of common stock reserved for issuance under our 2016 Employee Stock Purchase Plan as of September 30, 2018, (3) 986,100 shares of common stock reserved for issuance under our 2018 Equity Inducement Plan as of September 30, 2018;
- An increase in the number of shares of common stock approved by our stockholders pursuant to an amendment on October 8, 2018 to increase the number of shares available under the 2016 Equity Incentive Plan by 1,759,602 shares, which resulted in a total of 1,844,123 shares of common stock reserved and available for future issuance under the 2016 Equity Incentive Plan as of October 8, 2018. Of such 1,844,123 shares available for future issuance on October 8, 2018, options for an aggregate of 379,900 shares of common stock were granted after October 8, 2018, with a weighted average exercise price of \$9.26 per share; and

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- 1,845,820 shares of common stock sold under the at-the-market program with JonesTrading Institutional Services LLC in October 2018.

The foregoing table does not give effect to the exercise of any outstanding options or warrants. To the extent options and warrants are exercised, there may be further dilution to new investors.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Jefferies under which we may issue and sell shares of our common stock from time to time up to an aggregate sales price of \$60,000,000 through Jefferies. The sales agreement is filed as Exhibit 1.2 to our registration statement on Form S-3 of which this prospectus supplement forms a part, and is incorporated by reference in this prospectus supplement. Sales of our common stock, if any, under this prospectus supplement will be made by any method that is deemed an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act, including sales made directly on or through the Nasdaq Global Market or any other existing trading market for our common stock.

When requested by us, Jefferies will offer the shares of common stock subject to the terms and conditions of the sales agreement, which may be on a daily basis for periods of time, or as we may otherwise agree with Jefferies. We will designate the maximum amount of shares of common stock to be sold through Jefferies when we request Jefferies to do so. Jefferies has agreed, subject to the terms and conditions of the sales agreement, to use its commercially reasonable efforts to execute our orders to sell, as our sales agent and on our behalf, shares of our common stock submitted to Jefferies from time to time by us, consistent with its normal sales and trading practices. We may instruct Jefferies not to place shares of common stock at or below a price designated by us. We or Jefferies may suspend the offering of shares of common stock under the sales agreement upon proper notice to the other party.

If we and Jefferies so agree, Jefferies may act as principal in connection with the placement of the securities offered hereby.

We will pay Jefferies a commission of 3.0% of the gross proceeds of any shares sold through it pursuant to this prospectus supplement, and reimburse Jefferies for up to \$50,000 of its expenses, including fees and disbursements to its legal counsel. The estimated offering expenses payable by us, in addition to such commission and reimbursement of expenses, are approximately \$270,000, which includes legal, accounting and printing costs and various other fees associated with registering the shares of common stock. The remaining sale proceeds, after deducting any other transaction fees, will equal our net proceeds from the sale of such shares.

Jefferies will provide written confirmation to us following the close of trading on the Nasdaq Global Market each day on which shares of common stock are sold under the sales agreement. Each confirmation will include the number of shares sold on that day, the aggregate gross proceeds of such sales and the commission payable by us to Jefferies. Settlement for sales of common stock will occur, unless otherwise agreed, on the second business day following the date on which such sales were made.

In connection with the sale of our common stock on our behalf, Jefferies will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of Jefferies will be deemed to be underwriting commissions or discounts.

We have agreed to indemnify Jefferies against certain liabilities, including liabilities under the Securities Act. We have also agreed to contribute to payments Jefferies may be required to make in respect of such liabilities.

The offering of shares of common stock pursuant to the sales agreement will terminate upon the earliest of (i) the sale of all shares of common stock subject to the sales agreement and this prospectus supplement and (ii) the termination of the sales agreement according to its terms by either Jefferies or us.

Jefferies has provided, and may in the future provide, various investment banking, commercial banking, financial advisory and other services to us and our affiliates for which services it has received, and may in the future receive, customary fees. In the course of its business, Jefferies may actively trade our securities for its own account or for the accounts of customers, and, accordingly, Jefferies may at any time hold long or short positions in such securities.

LEGAL MATTERS

Fenwick & West LLP will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of Aeglea BioTherapeutics, Inc. Jefferies LLC is being represented in connection with this offering by Cooley LLP, New York, New York.

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.



Up to \$60,000,000

Common Stock

PROSPECTUS SUPPLEMENT

Jefferies

, 2018

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following table sets forth estimated expenses in connection with the issuance and distribution of the securities being registered:

SEC registration fee	\$23,595
FINRA filing fee	41,750
Printing and engraving*	*
Legal fees and expenses*	*
Accounting fees and expenses*	*
Transfer agent and registrar fees and expenses*	*
Miscellaneous expenses*	*
Total*	<u>\$</u> *

* These fees are calculated based on the type of securities offered and the number of issuances and accordingly, cannot be estimated at this time.

Item 15. Indemnification of Officers and Directors

Section 145 of the Delaware General Corporation Law authorizes a court to award, or a corporation's board of directors to grant, indemnity to directors and officers under certain circumstances and subject to certain limitations. The terms of Section 145 of the Delaware General Corporation Law are sufficiently broad to permit indemnification under certain circumstances for liabilities, including reimbursement of expenses incurred, arising under the Securities Act of 1933, as amended, or the Securities Act.

As permitted by the Delaware General Corporation Law, the Registrant's restated certificate of incorporation contains provisions that eliminate the personal liability of its directors for monetary damages for any breach of fiduciary duties as a director, except liability for the following:

- any breach of the director's duty of loyalty to the Registrant or its stockholders;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- under Section 174 of the Delaware General Corporation Law (regarding unlawful dividends and stock purchases); or
- any transaction from which the director derived an improper personal benefit.

As permitted by the Delaware General Corporation Law, the Registrant's restated bylaws provide that:

- the Registrant is required to indemnify its directors and executive officers to the fullest extent permitted by the Delaware General Corporation Law, subject to very limited exceptions;
- the Registrant may indemnify its other employees and agents as set forth in the Delaware General Corporation Law;
- the Registrant is required to advance expenses, as incurred, to its directors and executive officers in connection with a legal proceeding to the fullest extent permitted by the Delaware General Corporation Law, subject to very limited exceptions; and
- the rights conferred in the restated bylaws are not exclusive.

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The Registrant has entered, and intends to continue to enter, into separate indemnification agreements with its directors and executive officers to provide these directors and executive officers additional contractual assurances regarding the scope of the indemnification set forth in the Registrant's restated certificate of incorporation and restated bylaws and to provide additional procedural protections. At present, there is no pending litigation or proceeding involving a director or executive officer of the Registrant regarding which indemnification is sought. The indemnification provisions in the Registrant's restated certificate of incorporation, restated bylaws and the indemnification agreements entered into or to be entered into between the Registrant and each of its directors and executive officers may be sufficiently broad to permit indemnification of the Registrant's directors and executive officers for liabilities arising under the Securities Act.

The Registrant currently carries liability insurance for its directors and officers. One of the Registrant's directors, Armen Shanafelt, is also indemnified by his employer with regard to his service on the Registrant's board of directors.

Reference is made to the following documents filed as exhibits to this Registration Statement regarding relevant indemnification provisions described above and elsewhere herein:

<u>Exhibit</u>	<u>Number</u>
Restated Certificate of Incorporation	3.1
Restated Bylaws	3.2
Amended and Restated Investors' Rights Agreement, dated March 10, 2015, by and among the Registrant and certain of its stockholders, as amended	4.2

Item 16. Exhibits

The exhibits listed in the accompanying Exhibit Index are filed (except where otherwise indicated) as part of this Registration Statement.

Item 17. Undertakings

(a) The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) to include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) to reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Securities and Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) to include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that subparagraphs (i),(ii), and (iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Securities and Commission by the Registrant pursuant to Section 13 or Section 15(d) of the Securities

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Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(i) Each prospectus filed by the Registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(5) That, for the purpose of determining liability of the Registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned Registrant undertakes that in a primary offering of securities of the undersigned Registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned Registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) any preliminary prospectus or prospectus of the undersigned Registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) any free writing prospectus relating to the offering prepared by or on behalf of the undersigned Registrant or used or referred to by the undersigned Registrant;

(iii) the portion of any other free writing prospectus relating to the offering containing material information about the undersigned Registrant or its securities provided by or on behalf of the undersigned Registrant; and

(iv) any other communication that is an offer in the offering made by the undersigned Registrant to the purchaser.

(b) The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the Registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual

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report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(c) The undersigned Registrant hereby undertakes to deliver or cause to be delivered with the prospectus, to each person to whom the prospectus is sent or given, the latest annual report, to security holders that is incorporated by reference in the prospectus and furnished pursuant to and meeting the requirements of Rule 14a-3 or Rule 14c-3 under the Securities Exchange Act of 1934; and, where interim financial information required to be presented by Article 3 of Regulation S-X is not set forth in the prospectus, to deliver, or cause to be delivered to each person to whom the prospectus is sent or given, the latest quarterly report that is specifically incorporated by reference in the prospectus to provide such interim financial information.

(d) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers, and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer, or controlling person of the Registrant in the successful defense of any action, suit, or proceeding) is asserted by such director, officer, or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.

(e) If and when applicable, the Registrant hereby further undertakes to file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act in accordance with the rules and regulations prescribed by the Securities and Exchange Commission under Section 305(b)(2) of the Trust Indenture Act.

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EXHIBIT INDEX

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
1.1*	Form of Underwriting Agreement					
1.2	Open Market Sale AgreementSM, dated December 21, 2018, by and between the Registrant and Jefferies LLC					X
3.1	Restated Certificate of Incorporation	S-1/A	333-205001	3.2	9/14/2015	
3.2	Restated Bylaws	S-1/A	333-205001	3.4	9/14/2015	
4.1	Form of Common Stock Certificate	S-1/A	333-205001	4.1	9/14/2015	
4.2	Amended and Restated Investors' Rights Agreement, dated March 10, 2015, by and among the Registrant and certain of its stockholders, as amended	S-1	333-205001	4.2	6/16/2015	
4.3	Form of Debt Security					X
4.4	Form of Indenture					X
4.5*	Form of Warrant					
4.6*	Form of Warrant Agreement					
4.7*	Form of Preferred Stock Certificate					
4.8*	Form of Subscription Rights Certificate					
4.9*	Form of Unit					
4.10*	Form of Unit Agreement					
5.1	Opinion of Fenwick & West LLP					X
23.1	Consent of PricewaterhouseCoopers LLP					X
23.2	Consent of Fenwick & West LLP (included in Exhibit 5.1)					X
24.1	Power of Attorney (included on the signature page hereto)					X
25.1**	Form T-1 Statement of Eligibility of Trustee for Senior Indenture under the Trust Indenture Act of 1939.					
25.2**	Form T-1 Statement of Eligibility of Trustee for Subordinated Indenture under the Trust Indenture Act of 1939.					

* To be filed by amendment or as an exhibit to a report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended and incorporated herein by reference.

** To be filed in accordance with the requirements of Section 305(b)(2) of the Trust Indenture Act of 1939 and Rule 5b-3 thereunder.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Austin, State of Texas, on December 21, 2018.

AEGLEA BIOTHERAPEUTICS, INC.

By: /s/ Anthony G. Quinn, M.B Ch.B, Ph.D.
Anthony G. Quinn, M.B Ch.B, Ph.D.
Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Anthony G. Quinn, M.B Ch.B, Ph.D. and Charles N. York II, and each of them, as his true and lawful attorneys-in-fact, proxies and agents, each with full power of substitution, for him in any and all capacities, to sign any and all amendments to this registration statement (including post-effective amendments or any abbreviated registration statement and any amendments thereto filed pursuant to Rule 462(b) increasing the number of securities for which registration is sought), and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact, proxies and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully for all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact, proxies and agents, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Anthony G. Quinn, M.B Ch.B, Ph.D.</u> Anthony G. Quinn, M.B Ch.B, Ph.D.	Chief Executive Officer and Director (Principal Executive Officer)	December 21, 2018
<u>/s/ Charles N. York II</u> Charles N. York II	Chief Financial Officer and Vice President (Principal Accounting Officer and Principal Financial Officer)	December 21, 2018
<u>/s/ Suzanne L. Bruhn, Ph.D.</u> Suzanne L. Bruhn, Ph.D.	Director	December 21, 2018
<u>/s/ Russell J. Cox</u> Russell J. Cox	Director	December 21, 2018
<u>/s/ Ivana Magocevic-Liebisch, Ph.D.</u> Ivana Magocevic-Liebisch, Ph.D.	Director	December 21, 2018
<u>/s/ Sandesh Mahatme, LLM</u> Sandesh Mahatme, LLM	Director	December 21, 2018
<u>/s/ V. Bryan Lawlis, Ph.D.</u> V. Bryan Lawlis, Ph.D.	Director	December 21, 2018
<u>/s/ Armen Shanafelt, Ph.D.</u> Armen Shanafelt, Ph.D.	Director	December 21, 2018

OPEN MARKET SALE AGREEMENTSM

December 21, 2018

JEFFERIES LLC
520 Madison Avenue
New York, New York 10022

Ladies and Gentlemen:

Aglea BioTherapeutics, Inc., a Delaware corporation (the “**Company**”), proposes, subject to the terms and conditions stated herein, to issue and sell from time to time through Jefferies LLC, as sales agent and/or principal (the “**Agent**”), shares of the Company’s common stock, par value \$0.0001 per share (the “**Common Shares**”), on the terms set forth in this agreement (this “**Agreement**”).

Section 1. DEFINITIONS

(a) **Certain Definitions.** For purposes of this Agreement, capitalized terms used herein and not otherwise defined shall have the following respective meanings:

“**Affiliate**” of a Person means another Person that directly or indirectly, through one or more intermediaries, controls, is controlled by, or is under common control with, such first-mentioned Person. The term “control” (including the terms “controlling,” “controlled by” and “under common control with”) means the possession, direct or indirect, of the power to direct or cause the direction of the management and policies of a Person, whether through the ownership of voting securities, by contract or otherwise.

“**Agency Period**” means the period commencing on the date of this Agreement and expiring on the earliest to occur of (x) the date on which the Agent shall have placed the Maximum Program Amount pursuant to this Agreement and (y) the date this Agreement is terminated pursuant to Section 7.

“**Commission**” means the U.S. Securities and Exchange Commission.

“**Exchange Act**” means the Securities Exchange Act of 1934, as amended, and the rules and regulations of the Commission thereunder.

“**Floor Price**” means the minimum price set by the Company in the Issuance Notice below which the Agent shall not sell Shares during the applicable period set forth in the Issuance Notice, which may be adjusted by the Company at any time during the period set forth in the Issuance Notice by delivering written notice of such change to the Agent and which in no event shall be less than \$1.00 without the prior written consent of the Agent, which may be withheld in the Agent’s sole discretion.

SM “Open Market Sale Agreement” is a service mark of Jefferies LLC

“**Issuance Amount**” means the aggregate Sales Price of the Shares to be sold by the Agent pursuant to any Issuance Notice.

“**Issuance Notice**” means a written notice delivered to the Agent by the Company in accordance with this Agreement in the form attached hereto as Exhibit A that is executed by its Chief Executive Officer, President or Chief Financial Officer.

“**Issuance Notice Date**” means any Trading Day during the Agency Period that an Issuance Notice is delivered pursuant to Section 3(b)(i).

“**Issuance Price**” means the Sales Price less the Selling Commission.

“**Maximum Program Amount**” means Common Shares with an aggregate Sales Price of the lesser of (a) the number or dollar amount of Common Shares registered under the effective Registration Statement (defined below) pursuant to which the offering is being made, (b) the number of authorized but unissued Common Shares (less Common Shares issuable upon exercise, conversion or exchange of any outstanding securities of the Company or otherwise reserved from the Company’s authorized capital stock), (c) the number or dollar amount of Common Shares permitted to be sold under Form S-3 (including General Instruction I.B.6 thereof, if applicable), or (d) the number or dollar amount of Common Shares for which the Company has filed a Prospectus (defined below).

“**Person**” means an individual or a corporation, partnership, limited liability company, trust, incorporated or unincorporated association, joint venture, joint stock company, governmental authority or other entity of any kind.

“**Principal Market**” means the Nasdaq Global Market or such other national securities exchange on which the Common Shares, including any Shares, are then listed.

“**Sales Price**” means the actual sale execution price of each Share placed by the Agent pursuant to this Agreement.

“**Securities Act**” means the Securities Act of 1933, as amended, and the rules and regulations of the Commission thereunder.

“**Selling Commission**” means three percent (3.0%) of the gross proceeds of Shares sold pursuant to this Agreement, or as otherwise agreed between the Company and the Agent with respect to any Shares sold pursuant to this Agreement.

“**Settlement Date**” means the second business day following each Trading Day during the period set forth in the Issuance Notice on which Shares are sold pursuant to this Agreement, when the Company shall deliver to the Agent the amount of Shares sold on such Trading Day and the Agent shall deliver to the Company the Issuance Price received on such sales.

“**Shares**” shall mean the Company’s Common Shares issued or issuable pursuant to this Agreement.

“**Trading Day**” means any day on which the Principal Market is open for trading.

Section 2. REPRESENTATIONS AND WARRANTIES OF THE COMPANY

The Company represents and warrants to, and agrees with, the Agent that as of (1) the date of this Agreement, (2) each Issuance Notice Date, (3) each Settlement Date, (4) each Triggering Event Date and (5) as of each Time of Sale (each of the times referenced above is referred to herein as a “**Representation Date**”), except as may be disclosed in the Prospectus (including any documents incorporated by reference therein and any supplements thereto) on or before a Representation Date:

(a) **Registration Statement.** The Company has prepared and filed or will file with the Commission a shelf registration statement on Form S-3 that contains a base prospectus (the “**Base Prospectus**”). Such registration statement registers the issuance and sale by the Company of the Shares under the Securities Act. The Company may file one or more additional registration statements from time to time that will contain a base prospectus and related prospectus or prospectus supplement, if applicable, with respect to the Shares. Except where the context otherwise requires, such registration statement(s), including any information deemed to be a part thereof pursuant to Rule 430B under the Securities Act, including all financial statements, exhibits and schedules thereto and all documents incorporated or deemed to be incorporated therein by reference pursuant to Item 12 of Form S-3 under the Securities Act as from time to time amended or supplemented, is herein referred to as the “**Registration Statement**,” and the prospectus constituting a part of such registration statement(s), together with any prospectus supplement filed with the Commission pursuant to Rule 424(b) under the Securities Act relating to a particular issuance of the Shares, including all documents incorporated or deemed to be incorporated therein by reference pursuant to Item 12 of Form S-3 under the Securities Act, in each case, as from time to time amended or supplemented, is referred to herein as the “**Prospectus**,” except that if any revised prospectus is provided to the Agent by the Company for use in connection with the offering of the Shares that is not required to be filed by the Company pursuant to Rule 424(b) under the Securities Act, the term “**Prospectus**” shall refer to such revised prospectus from and after the time it is first provided to the Agent for such use. The Registration Statement at the time it originally became effective is herein called the “**Original Registration Statement**.” As used in this Agreement, the terms “amendment” or “supplement” when applied to the Registration Statement or the Prospectus shall be deemed to include the filing by the Company with the Commission of any document under the Exchange Act after the date hereof that is or is deemed to be incorporated therein by reference.

All references in this Agreement to financial statements and schedules and other information which is “contained,” “included” or “stated” in the Registration Statement or the Prospectus (and all other references of like import) shall be deemed to mean and include all such financial statements and schedules and other information which is or is deemed to be incorporated by reference in or otherwise deemed under the Securities Act to be a part of or included in the Registration Statement or the Prospectus, as the case may be, as of any specified date; and all references in this Agreement to amendments or supplements to the Registration Statement or the

Prospectus shall be deemed to mean and include, without limitation, the filing of any document under the Exchange Act which is or is deemed to be incorporated by reference in or otherwise deemed under the Securities Act to be a part of or included in the Registration Statement or the Prospectus, as the case may be, as of any specified date. The Company's obligations under this Agreement to furnish, provide, deliver or make available (and all other references of like import) copies of any report or statement shall be deemed satisfied if the same is filed with the Commission through EDGAR.

At the time the Original Registration Statement was or will be declared effective and at the time the Company's most recent annual report on Form 10-K was filed with the Commission, if later, the Company met the then-applicable requirements for use of Form S-3 under the Securities Act. During the Agency Period, each time the Company files an annual report on Form 10-K the Company will meet the then-applicable requirements for use of Form S-3 under the Securities Act.

(b) Compliance with Registration Requirements. The Original Registration Statement and any Rule 462(b) Registration Statement have been or will be declared effective by the Commission under the Securities Act. The Company has complied or will comply with the Commission's satisfaction with all requests of the Commission for additional or supplemental information, if any. No stop order suspending the effectiveness of the Registration Statement or any Rule 462(b) Registration Statement is in effect and no proceedings for such purpose have been instituted or are pending or, to the best knowledge of the Company, are contemplated or threatened by the Commission.

The Prospectus when filed complied or will comply in all material respects with the Securities Act and, if filed with the Commission through its Electronic Data Gathering, Analysis and Retrieval system ("**EDGAR**") (except as may be permitted by Regulation S-T under the Securities Act), was identical to the copy thereof delivered to the Agent for use in connection with the issuance and sale of the Shares. Each of the Registration Statement, any Rule 462(b) Registration Statement and any post-effective amendment thereto, at the time it became or becomes effective and at each Representation Date, complied and will comply in all material respects with the Securities Act and did not and will not contain any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading. As of the date of this Agreement, the Prospectus and any Free Writing Prospectus considered together (collectively, the "**Time of Sale Information**") did not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading. The Prospectus, as amended or supplemented, as of its date and at each Representation Date, did not and will not contain any untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading. The representations and warranties set forth in the three immediately preceding sentences do not apply to statements in or omissions from the Registration Statement, any Rule 462(b) Registration Statement, or any post-effective amendment thereto, or the Prospectus, or any amendments or supplements thereto, made in reliance upon and in conformity with information relating to the Agent furnished to the Company in writing by the Agent expressly for use therein, it being understood and agreed that the only such information furnished by the Agent to the Company consists of the information described in

Section 6 below. There are no contracts or other documents required to be described in the Prospectus or to be filed as exhibits to the Registration Statement which have not been described or filed as required. The Registration Statement and the offer and sale of the Shares as contemplated hereby meet the requirements of Rule 415 under the Securities Act and comply in all material respects with said rule.

(c) Ineligible Issuer Status. The Company is not an “ineligible issuer” in connection with the offering of the Shares pursuant to Rules 164, 405 and 433 under the Securities Act. Any Free Writing Prospectus that the Company is required to file pursuant to Rule 433(d) under the Securities Act has been, or will be, filed with the Commission in accordance with the requirements of the Securities Act. Each Free Writing Prospectus that the Company has filed, or is required to file, pursuant to Rule 433(d) under the Securities Act or that was prepared by or on behalf of or used or referred to by the Company complies or will comply in all material respects with the requirements of Rule 433 under the Securities Act including timely filing with the Commission or retention where required and legending, and each such Free Writing Prospectus, as of its issue date and at all subsequent times through the completion of the issuance and sale of the Shares did not, does not and will not include any information that conflicted, conflicts with or will conflict with the information contained in the Registration Statement or the Prospectus, including any document incorporated by reference therein. Except for the Free Writing Prospectuses, if any, and electronic road shows, if any, furnished to the Agent before first use, the Company has not prepared, used or referred to, and will not, without the Agent’s prior consent, prepare, use or refer to, any Free Writing Prospectus.

(d) Incorporated Documents. The documents incorporated or deemed to be incorporated by reference in the Registration Statement and the Prospectus, at the time they were filed with the Commission, complied in all material respects with the requirements of the Exchange Act, as applicable, and, when read together with the other information in the Prospectus, do not contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein, in light of the circumstances under which they were made, not misleading.

(e) Exchange Act Compliance. The documents incorporated or deemed to be incorporated by reference in the Prospectus, at the time they were or hereafter are filed with the Commission, and any Free Writing Prospectus or amendment or supplement thereto complied and will comply in all material respects with the requirements of the Exchange Act, and, when read together with the other information in the Prospectus, at the time the Registration Statement and any amendments thereto become effective and as of each Representation Date, as the case may be, will not contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the fact required to be stated therein or necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading.

(f) Emerging Growth Company. From the time of the Company’s initial public offering through the date hereof, the Company has been and is an “emerging growth company,” as defined in Section 2(a) of the Securities Act (an “**Emerging Growth Company**”).

(g) Organization and Good Standing. The Company and each of its subsidiaries (listed on Exhibit 21.1 to the Company's most recent annual report on Form 10-K) have been duly organized and are validly existing as corporations or other legal entities in good standing (or the foreign equivalent thereof) under the laws of their respective jurisdictions of organization. The Company and each of its subsidiaries are duly qualified to do business and are in good standing (to the extent the concept of good standing or a functional equivalent is recognized in such jurisdictions) as foreign corporations or other legal entities in each jurisdiction in which their respective ownership or lease of property or the conduct of their respective businesses requires such qualification and have all power and authority (corporate or other) necessary to own or hold their respective properties and to conduct the businesses in which they are engaged, except where the failure to so qualify or have such power or authority would not reasonably be expected to (i) have, singularly or in the aggregate, a material adverse effect on the condition (financial or otherwise), results of operations or prospects of the Company and its subsidiaries taken as a whole, or (ii) impair in any material respect the ability of the Company to perform its obligations under this Agreement or to consummate any transactions contemplated by this Agreement or the Prospectus (any such effect as described in clauses (i) or (ii), a "**Material Adverse Effect**"). The subsidiaries listed on Exhibit 21.1 to the Company's most recent annual report on Form 10-K are the only significant subsidiaries of the Company.

(h) This Agreement. This Agreement has been duly authorized, executed and delivered, and is a valid and binding agreement of the Company, enforceable in accordance with its terms, except as rights to indemnification hereunder may be limited by applicable law and except as the enforcement hereof may be limited by bankruptcy, insolvency, reorganization, moratorium or other similar laws relating to or affecting the rights and remedies of creditors or by general equitable principles.

(i) The Shares. The Shares have been duly and validly authorized and, when issued and delivered against payment therefor as provided herein, will be duly and validly issued, fully paid and non-assessable and will conform in all material respects to the descriptions thereof in the Registration Statement and the Prospectus; and the issuance of the Shares is not subject to any preemptive, rights of first refusal or similar rights

(j) Capitalization. The Company has an authorized capitalization as set forth in the Company's most recent financial statements incorporated by reference in the Prospectus, and all of the issued shares of capital stock of the Company have been duly and validly authorized and issued, are fully paid and non-assessable, have been issued in compliance with federal and state securities laws, and conform to the description thereof contained or incorporated by reference in the Prospectus. All of the Company's options, warrants and other rights to purchase or exchange any securities for shares of the Company's capital stock have been duly authorized and validly issued and were issued in compliance with federal and state securities laws. None of the outstanding Common Shares were issued in violation of any preemptive rights, rights of first refusal or other similar rights to subscribe for or purchase securities of the Company. As of the date hereof, there are no authorized or outstanding shares of capital stock, options, warrants, preemptive rights, rights of first refusal or other rights to purchase, or equity or debt securities convertible into or exchangeable or exercisable for, any capital stock of the Company or any of its subsidiaries other than those described above or accurately described in all material respects in the Registration Statement and Prospectus. The description of the Company's stock option, stock bonus and other stock plans or arrangements, and the options or other rights granted thereunder, as described in the Prospectus, accurately and fairly present in all material respects the information required to be shown with respect to such plans, arrangements, options and rights.

(k) Capitalization of Subsidiaries. All the outstanding shares of capital stock (if any) of each subsidiary of the Company have been duly authorized and validly issued, are fully paid and nonassessable and, except to the extent set forth in the Registration Statement or the Prospectus, are owned by the Company directly or indirectly through one or more wholly-owned subsidiaries, free and clear of any claim, lien, encumbrance, security interest, restriction upon voting or transfer or any other claim of any third party.

(l) No Conflicts. The execution, delivery and performance of this Agreement by the Company, the issuance and sale of the Shares by the Company and the consummation of the transactions contemplated hereby will not (with or without notice or lapse of time or both) (i) conflict with or result in a breach or violation of any of the terms or provisions of, constitute a default or a Debt Repayment Triggering Event (as defined below) under, or result in the creation or imposition of any lien, encumbrance, security interest, claim or charge upon any property or assets of the Company or any subsidiary pursuant to, any indenture, mortgage, deed of trust, loan agreement or other agreement or instrument to which the Company or any of its subsidiaries is a party or by which the Company or any of its subsidiaries is bound or to which any of the property or assets of the Company or any of its subsidiaries is subject, (ii) result in any violation of the provisions of the charter or by-laws (or analogous governing instruments, as applicable) of the Company or any of its subsidiaries or (iii) result in the violation of any law, statute, rule, regulation, judgment, order or decree of any court or governmental or regulatory agency or body, domestic or foreign, having jurisdiction over the Company or any of its subsidiaries or any of their properties or assets except, in the case of clauses (i), (ii) and (iii) above, for any such conflict, breach, violation or default that would not, individually or in the aggregate, have a Material Adverse Effect. A “**Debt Repayment Triggering Event**” means any event or condition that gives, or with the giving of notice or lapse of time would give the holder of any note, debenture or other evidence of indebtedness (or any person acting on such holder’s behalf) the right to require the repurchase, redemption or repayment of all or a portion of such indebtedness by the Company of any of its subsidiaries.

(m) No Consents Required. Except for the registration of the Shares under the Securities Act, the Exchange Act and applicable state securities laws, and such consents, approvals, authorizations, orders and registrations or qualifications as may be required by the Financial Industry Regulatory Authority (“**FINRA**”) and the Principal Market in connection with the purchase and distribution of the Shares by the Agent and the listing of the Shares on the Principal Market, no consent, approval, authorization or order of, or filing, qualification or registration with, any court, governmental or regulatory agency or body, foreign or domestic, which has not been made, obtained or taken and is not in full force and effect, is required for the execution, delivery and performance of this Agreement by the Company, the issuance and sale of the Shares or the consummation of the transactions contemplated hereby; and no event has occurred that allows or results in, or after notice or lapse of time or both would allow or result in, revocation, suspension, termination or invalidation of any such consent, approval, authorization or order of, or filing, qualification or registration or any other impairment of the rights of the holder or maker of any such consent, approval, authorization or order of, or filing, qualification or registration.

(n) Independent Auditors. PricewaterhouseCoopers LLP, who have certified certain financial statements of the Company and its consolidated subsidiaries included or incorporated by reference in the Registration Statement and the Prospectus, is an independent registered public accounting firm with respect to the Company and its consolidated subsidiaries within the meaning of Article 2-01 of Regulation S-X and the Public Company Accounting Oversight Board (United States) (the “PCAOB”).

(o) Financial Statements. The financial statements, together with the related notes, included or incorporated by reference in the Prospectus and in the Registration Statement fairly present the financial position and the results of operations and changes in financial position of the Company and its consolidated subsidiaries at the respective dates or for the respective periods therein specified. Such statements and related notes have been prepared in accordance with the generally accepted accounting principles in the United States (“GAAP”) applied on a consistent basis throughout the periods involved except as may be set forth in the related notes included or incorporated by reference in the Prospectus; and provided that the unaudited interim financial statements, which are subject to normal year-end adjustments, may not contain certain footnotes, as permitted by the applicable rules of the Commission. The financial statements, together with the related notes, included or incorporated by reference in the Prospectus comply in all material respects with Regulation S-X. No other financial statements or supporting schedules or exhibits are required by Regulation S-X to be described, included or incorporated by reference in the Registration Statement or the Prospectus. The summary and selected financial data included or incorporated by reference in the Prospectus and the Registration Statement fairly present in all material respects the information shown therein as at the respective dates and for the respective periods specified and are derived from the consolidated financial statements set forth in the Registration Statement and the Prospectus and other financial information.

(p) Off-Balance Sheet Transactions. Except as described in the Registration Statement and the Prospectus, there are no material off-balance sheet transactions (including, without limitation, transactions related to, and the existence of, “variable interest entities” within the meaning of Financial Accounting Standards Board Accounting Standards Codification Topic 810), arrangements, obligations (including contingent obligations), or any other relationships with unconsolidated entities or other persons, that may reasonably be expected to have a material current or future effect on the Company’s financial condition, changes in financial condition, results of operations, liquidity, capital expenditures, capital resources, or significant components of revenues or expenses.

(q) No Material Adverse Change. Neither the Company nor any of its subsidiaries has sustained, since the date of the latest audited financial statements included or incorporated by reference in the Registration Statement or the Prospectus, (i) any material loss or interference with its business from fire, explosion, flood or other calamity, whether or not covered by insurance, or from any labor dispute or action, order or decree of any court or governmental or regulatory authority, otherwise than as set forth or contemplated in the Registration Statement and the Prospectus; (ii) any change in the capital stock (other than the issuance of Common Shares upon exercise of stock options and warrants described as outstanding in, and the grant of

options and awards under existing equity incentive plans described in, the Registration Statement and the Prospectus) or long-term debt of the Company or any of its subsidiaries, or any dividend or distribution of any kind declared, set aside for payment, paid or made by the Company on any class of capital stock, or any material adverse change, or any development involving a prospective material adverse change, in or affecting the business, properties, assets, general affairs, management, financial position, prospects, stockholders' equity or results of operations of the Company and its subsidiaries taken as a whole, otherwise than as set forth or contemplated in the Registration Statement and the Prospectus.

(r) Legal Proceedings. Except as set forth in the Registration Statement and the Prospectus, there is no legal or governmental proceeding to which the Company or any of its subsidiaries is a party or of which any property or assets of the Company or any of its subsidiaries is the subject, including any proceeding before the United States Food and Drug Administration of the U.S. Department of Health and Human Services ("FDA"), European Medicines Agency ("EMA"), Medicines and Health Products Regulatory Agency ("MHRA") or other comparable federal, state, local or foreign governmental bodies (it being understood that the interaction between the Company and the FDA and such comparable governmental bodies relating to the clinical development and product approval process shall not be deemed proceedings for purposes of this representation), which is required to be described in the Registration Statement or the Prospectus or a document incorporated by reference therein and is not described therein, or which, singularly or in the aggregate, if determined adversely to the Company or any of its subsidiaries, would reasonably be expected to have a Material Adverse Effect; and to the Company's knowledge, no such proceedings are threatened or, contemplated by governmental or regulatory authorities or threatened by others. The Company is in compliance with all applicable federal, state, local and foreign laws, regulations, orders and decrees governing its business as prescribed by the FDA, or any other federal, state or foreign agencies or bodies engaged in the regulation of pharmaceuticals or biohazardous substances or materials, except where noncompliance would not, singly or in the aggregate, have a Material Adverse Effect. All nonclinical studies and clinical trials conducted by or on behalf of the Company to support approval for commercialization of the Company's product candidates have been and/or are being conducted by the Company, or to the Company's knowledge by third parties, in compliance with all applicable federal, state or foreign laws, rules, orders and regulations, except for such failure or failures to be in compliance as would not reasonably be expected to have, singly or in the aggregate, a Material Adverse Effect.

(s) No Violation or Default. Neither the Company nor any of its subsidiaries is (i) in violation of its charter or by-laws (or analogous governing instrument, as applicable), (ii) in default in any respect, and no event has occurred which, with notice or lapse of time or both, would constitute such a default, in the due performance or observance of any term, covenant or condition contained in any indenture, mortgage, deed of trust, loan agreement, lease or other agreement or instrument to which it is a party or by which it is bound or to which any of its property or assets is subject (including, without limitation, those administered by the FDA, EMA, MHRA or by any other foreign, federal, state or local governmental or regulatory authority performing functions similar to those performed by the FDA, EMA or MHRA) or (iii) in violation in any respect of any law, ordinance, governmental rule, regulation or court order, decree or judgment to which it or its property or assets may be subject except, in the case of clauses (ii) and (iii) above, for any such violation or default that would not reasonably be expected to, singularly or in the aggregate, have a Material Adverse Effect.

(t) Licenses or Permits. The Company and each of its subsidiaries possess all licenses, certificates, authorizations and permits issued by, and have made all declarations and filings with, the appropriate local, state, federal or foreign governmental or regulatory agencies or bodies (including, without limitation, those administered by the FDA, EMA, MHRA or by any other foreign, federal, state or local governmental or regulatory authority performing functions similar to those performed by the FDA, EMA or MHRA) that are necessary to conduct of their respective businesses as described in the Prospectus (collectively, the “**Governmental Permits**”) except where any failures to possess or make the same would not, singularly or in the aggregate, reasonably be expected to have a Material Adverse Effect. The Company and its subsidiaries are in compliance with all such Governmental Permits; all such Governmental Permits are valid and in full force and effect, except where the validity or failure to be in full force and effect would not, individually or in the aggregate, have a Material Adverse Effect. Neither the Company nor any subsidiary has received notification of any revocation, adverse modification, suspension, termination or invalidation (or proceedings related thereto) of any such Governmental Permit and the Company has no reason to believe that any such Governmental Permit will not be renewed.

(u) Regulatory Matters: Clinical Trials. The nonclinical studies and clinical trials conducted by or on behalf of the Company that are described in the Prospectus (the “**Company Studies**”) were and, if still pending, are being, conducted in all material respects in accordance with their experimental protocols; the descriptions of the results of the Company Studies contained in the Prospectus are accurate in all material respects; the Company has no knowledge of any other nonclinical studies or clinical trials not described in the Prospectus, the results of which are inconsistent with or otherwise call into question the results described or referred to in the Prospectus; and the Company has not received any written notices or correspondence with the FDA, EMA, MHRA or any other foreign, state or local governmental body exercising comparable authority requiring the termination, suspension or material modification of any Company Studies that termination, suspension or material modification would reasonably be expected to have a Material Adverse Effect and, to the Company’s knowledge, there are no reasonable grounds for the same. To the Company’s knowledge, none of the Company Studies involved any investigator who has been disqualified as a clinical investigator or has been found by the FDA, EMA or MHRA to have engaged in scientific misconduct.

(v) Regulatory Matters: Manufacturing. To the Company’s knowledge, the manufacturing facilities and operations of its suppliers are operated in compliance in all material respects with all applicable statutes, rules, regulations and policies of the FDA and comparable regulatory agencies outside of the United States (including the EMA and MHRA) to which the Company is subject.

(w) Investment Company Act. The Company is not nor, after giving effect to the offering of the Shares and the application of the net proceeds thereof as described in the Prospectus, will it be required to register as an “investment company” or an entity “controlled” by an “investment company” within the meaning of the Investment Company Act of 1940, as amended, and the rules and regulations of the Commission thereunder.

(x) **No Stabilization.** Neither the Company nor, to the Company's knowledge, any of its officers, directors or affiliates has taken or will take, directly or indirectly, any action designed or intended to stabilize or manipulate the price of any security of the Company, or which caused or resulted in, or which might in the future reasonably be expected to cause or result in, stabilization or manipulation of the price of any security of the Company.

(y) **Intellectual Property.** The Company and its subsidiaries own or possess the valid rights to use all (i) trademarks, trademark registrations, service marks, Internet domain name registrations, and all goodwill associated with the foregoing, patents, patent applications, copyrights, copyright registrations and trade secrets (the "**Intellectual Property Rights**") and (ii) inventions, software, works of authorship, trade names, know-how, databases, formulae, Internet domain names, and other intellectual property (including unpatented and/or unpatentable proprietary or confidential information, systems, or procedures) (collectively, "**Intellectual Property Assets**") necessary to conduct their respective businesses as currently conducted and described in the Prospectus; provided that the foregoing representation is made only to the Company's knowledge as it concerns third-party Intellectual Property Rights and Intellectual Property Assets. The Company and its subsidiaries have not received any written opinion from their legal counsel concluding that any activities of their respective businesses, each as currently conducted, infringe, misappropriate, or otherwise violate valid and enforceable Intellectual Property Rights of any third party, and the Company and its subsidiaries have not received written notice of any pending or threatened action, suit, proceeding or claim by any third party challenging the Company's and its subsidiaries' rights in or to any of their respective Intellectual Property Rights or Intellectual Property Assets owned or used by the Company or its subsidiaries. To the Company's knowledge, the Company and its subsidiaries' respective businesses do not infringe, misappropriate or otherwise violate any Intellectual Property Rights of any third party. All licenses for the use of the Intellectual Property Rights by the Company described in the Prospectus are valid, binding upon, and enforceable against the Company and, to the Company's knowledge, the other parties thereto in accordance to its terms. The Company and its subsidiaries have complied in all material respects with, and are not in breach in any material respect nor have received any written asserted or threatened claim of breach of any intellectual property license, and the Company and its subsidiaries have no knowledge of any breach or anticipated breach by any third party with respect to any intellectual property license to which the Company is a party. The Company and its subsidiaries have taken commercially reasonable steps to protect, maintain and safeguard their Intellectual Property Rights sufficient, in the Company's reasonable business judgment, for the conduct of their businesses as currently conducted and described in the Prospectus, including the execution of appropriate nondisclosure and confidentiality agreements. The consummation of the transactions contemplated by this Agreement will not result in the loss or impairment of or payment of any additional amounts with respect to, nor require the consent of any third party in respect of, the Company's and its subsidiaries' right to own, use, or hold for use any of the material Intellectual Property Rights as owned, used or held for use in the conduct of their business as currently conducted. The Company and its subsidiaries have at all times complied in all material respects with all applicable laws relating to privacy, data protection, and the collection and use of personal information collected, used, or held for use by the Company in the conduct of the Company's business. To the Company's knowledge, no claims have been asserted or threatened against the Company or its subsidiaries alleging a violation of any person's privacy or personal information or data rights and the consummation of the transactions contemplated hereby will not breach or

otherwise cause any violation of any law related to privacy, data protection, or the collection and use of personal information collected, used, or held for use by the Company or its subsidiaries in the conduct of their businesses, except where any such breach or violation would not reasonably be expected to result in a Material Adverse Effect. The Company and its subsidiaries take commercially reasonable measures to ensure that such information is protected against unauthorized access, use, modification, or other misuse. The Company and its subsidiaries have used commercially reasonable efforts to obtain ownership of all works of authorship and inventions made by their employees, consultants and contractors during the time they were employed by or under contract with the Company and its subsidiaries and which are material to their businesses. All founders and key employees have signed confidentiality and invention assignment agreements with the Company or its applicable subsidiary.

(z) Title to Real and Personal Property. The Company and each of its subsidiaries have good and marketable title in fee simple (in the case of real property), or have valid rights to lease or otherwise use, all items of real or personal property (provided, that for the sake of clarity, rights to Intellectual Property Rights and Intellectual Property Assets are addressed exclusively in Section 2(y) above) which are material to the business of the Company and its subsidiaries taken as a whole, in each case free and clear of all liens, encumbrances, security interests, claims and defects other than those described in the Prospectus and those that do not, singularly or in the aggregate, materially affect the value of such property and do not materially interfere with the use made and proposed to be made of such property by the Company or any of its subsidiaries or could not reasonably be expected, singularly or in the aggregate, to have a Material Adverse Effect.

(aa) No Labor Dispute. There is (A) no significant unfair labor practice complaint pending against the Company, or any of its subsidiaries, nor to the Company's knowledge, threatened against it or any of its subsidiaries, before the National Labor Relations Board, any state or local labor relation board or any foreign labor relations board, and no significant grievance or significant arbitration proceeding arising out of or under any collective bargaining agreement is so pending against the Company or any of its subsidiaries, or, to the Company's knowledge, threatened against it and (B) no labor disturbance by or dispute with, the employees of the Company or any of its subsidiaries exists or, to the Company's knowledge, is contemplated or threatened, and the Company is not aware of any existing or imminent labor disturbance by the employees of any of its or its subsidiaries' principal suppliers, manufacturers, customers or contractors, that could reasonably be expected, singularly or in the aggregate, to have a Material Adverse Effect. The Company is not aware that any key employee or significant group of employees of the Company or any subsidiary plans to terminate employment with the Company or any such subsidiary.

(bb) Compliance with ERISA. No "prohibited transaction" (as defined in Section 406 of the Employee Retirement Income Security Act of 1974, as amended, including the regulations and published interpretations thereunder ("ERISA"), or Section 4975 of the Internal Revenue Code of 1986, as amended from time to time (the "Code")) or "accumulated funding deficiency" (as defined in Section 302 of ERISA) or any of the events set forth in Section 4043(b) of ERISA (other than events with respect to which the thirty (30)-day notice requirement under Section 4043 of ERISA has been waived) has occurred or would reasonably be expected to occur with respect to any "employee benefit plan" (as defined under ERISA) of the Company or any of its

subsidiaries which would, singularly or in the aggregate, reasonably be expected to have a Material Adverse Effect. Each employee benefit plan of the Company or any of its subsidiaries is in compliance in all material respects with applicable law, including ERISA and the Code. The Company and its subsidiaries have not incurred and would not reasonably be expected to incur material liability under Title IV of ERISA with respect to the termination of, or withdrawal from, any pension plan (as defined in ERISA). Each pension plan for which the Company or any of its subsidiaries would have any liability that is intended to be qualified under Section 401(a) of the Code is so qualified, and to the Company's knowledge, nothing has occurred, whether by action or by failure to act, which would, singularly or in the aggregate, reasonably be expected to cause the loss of such qualification.

(cc) Environmental Laws and Hazardous Materials. The Company and its subsidiaries are in compliance in all material respects with all foreign, federal, state and local rules, laws and regulations relating to the use, treatment, storage and disposal of hazardous or toxic substances or waste and protection of health and safety or the environment which are applicable to their businesses as described in the Registration Statement and the Prospectus ("**Environmental Laws**"). There has been no storage, generation, transportation, handling, treatment, disposal, discharge, emission, or other release of any kind of toxic or other hazardous wastes by, due to, or caused by the Company or any of its subsidiaries (or, to the Company's knowledge, any other entity for whose acts or omissions the Company or any of its subsidiaries is or may otherwise be liable) upon any of the property now or previously owned or leased by the Company or any of its subsidiaries, or upon any other property, in violation of any applicable law, statute, ordinance, rule, regulation, order, judgment, decree or permit or which would, under any applicable law, statute, ordinance, rule (including rule of common law), regulation, order, judgment, decree or permit, give rise to any liability that would reasonably be expected to have a Material Adverse Effect; and to the Company's knowledge, there has been no disposal, discharge, emission or other release of any kind onto such property or into the environment surrounding such property of any toxic or other hazardous wastes with respect to which the Company or any of its subsidiaries has knowledge and which would have a Material Adverse Effect.

(dd) Taxes. The Company and its subsidiaries each (i) have timely filed all necessary federal, state, local and foreign tax returns (or timely filed extensions with respect to such returns), and all such returns were true, complete and correct in all material respects, (ii) have paid all federal, state, local and foreign taxes, for which it is liable, including, without limitation, all sales and use taxes and all taxes which the Company or any of its subsidiaries is obligated to withhold from amounts owing to employees, creditors and third parties (other than such amounts being disputed in good faith and by appropriate proceedings and for which appropriate reserves, if required, have been established), and (iii) do not have any tax deficiency or claims outstanding or assessed or, to its knowledge, proposed against any of them, except those, in each of the cases described in clauses (i), (ii) and (iii) above, that would not, singularly or in the aggregate, have a Material Adverse Effect.

(ee) Insurance. The Company and each of its subsidiaries carry, or are covered by, insurance in such amounts and covering such risks as the Company reasonably believes is adequate for the conduct of their respective businesses as described in the Registration Statement and the Prospectus, and the value of their respective properties and is customary for companies engaged in similar businesses in similar industries. Neither the Company nor any of its

subsidiaries has any reason to believe that it will not be able to renew its existing insurance coverage as and when such coverage expires or to obtain similar coverage from similar insurers as may be necessary to continue its business at a cost that would not have a Material Adverse Effect. Neither the Company nor any of its subsidiaries has received written notice from any insurer, agent of such insurer or the broker of the Company or any of its subsidiaries that any material capital improvements or any other material expenditures (other than premium payments) are required or necessary to be made in order to continue such insurance.

(ff) Accounting Controls. The Company and each of its subsidiaries maintains a system of “internal control over financial reporting” (as such term is defined in Rule 13a-15(f) of the General Rules and Regulations under the Exchange Act (the “**Exchange Act Rules**”)) that is designed to comply in all material respects with any applicable requirements of the Exchange Act and has been designed by their respective principal executive and principal financial officers, or under their supervision, to provide reasonable assurances that (i) transactions are executed in accordance with management’s general or specific authorizations; (ii) transactions are recorded as necessary to permit preparation of financial statements in conformity with GAAP and to maintain accountability for assets; (iii) access to assets is permitted only in accordance with management’s general or specific authorization; (iv) the recorded accountability for assets is compared with existing assets at reasonable intervals and appropriate action is taken with respect to any differences; and (v) interactive data in eXtensible Business Reporting Language included or incorporated by reference in the Registration Statement fairly presents the Commission’s rules and guidelines applicable thereto. Except as described in the Registration Statement and the Prospectus, since the end of the Company’s most recent audited fiscal year, there has been (A) no material weakness in the Company’s internal control over financial reporting (whether or not remediated) and (B) no change in the Company’s internal control over financial reporting that has materially affected, or is reasonably likely to materially affect, the Company’s internal control over financial reporting.

(gg) Disclosure Controls. The Company and its subsidiaries maintain disclosure controls and procedures (as such is defined in Rule 13a-15(e) of the Exchange Act Rules) that comply with the requirements of the Exchange Act; such disclosure controls and procedures have been reasonably designed to ensure that information required to be disclosed by the Company and its subsidiaries in reports that they file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified by the Commission’s rules and forms, including controls and procedures designed to ensure that such information is accumulated and communicated to the Company’s management to allow timely decisions regarding disclosure. The Company and its subsidiaries have conducted evaluations of the effectiveness of their disclosure controls and procedures as required by Rule 13a-15 of the Exchange Act.

(hh) Minute Books. The minute books of the Company and each of its subsidiaries have been made available to the Agent and counsel for the Agent, and such books (i) contain a complete summary, in all material respects, of all meetings and actions of the board of directors (including each board committee) and stockholders of the Company (or analogous governing bodies and interest holders, as applicable), and each of its subsidiaries since the time of its respective incorporation or organization through the date of the latest meeting and action, and (ii) accurately in all material respects reflect all transactions referred to in such minutes.

(ii) No Undisclosed Relationships. No relationship, direct or indirect, exists between or among the Company or any of its subsidiaries on the one hand, and the directors, officers, stockholders (or analogous interest holders), customers or suppliers of the Company or any of its affiliates on the other hand, which is required to be described in the Prospectus and which is not so described.

(jj) No Registration Rights. There are no persons with registration rights or similar rights to have any securities registered for sale under the Registration Statement or included in the offering contemplated by this Agreement, other than those disclosed in the Registration Statement and the Prospectus and have been waived.

(kk) No Broker's Fees. The Company is not a party to any contract, agreement or understanding with any person (other than this Agreement) that would give rise to a valid claim against the Company or the Agent for a brokerage commission, finder's fee or like payment in connection with the offering and sale of the Shares or any transaction contemplated by this Agreement, the Registration Statement or the Prospectus.

(ll) No Restrictions on Subsidiaries. Except as described in Prospectus, no subsidiary of the Company is currently prohibited, directly or indirectly, under any agreement or other instrument to which it is a party or is subject, from paying any dividends to the Company, from making any other distribution on such subsidiary's capital stock, from repaying to the Company any loans or advances to such subsidiary from the Company or from transferring any of such subsidiary's properties or assets to the Company or any other subsidiary of the Company.

(mm) Forward-Looking Statements. No forward-looking statement (within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act) contained in either the Registration Statement or the Prospectus has been made or reaffirmed without a reasonable basis or has been disclosed other than in good faith.

(nn) Listing. The Company is subject to and in compliance in all material respects with the reporting requirements of Section 13 or Section 15(d) of the Exchange Act. The Common Shares are registered pursuant to Section 12(b) or 12(g) of the Exchange Act and is listed on the Principal Market, and the Company has taken no action designed to, or reasonably likely to have the effect of, terminating the registration of the Common Shares under the Exchange Act or delisting the Common Shares from the Principal Market, nor has the Company received any notification that the Commission or the Financial Industry Regulatory Authority ("FINRA") is contemplating terminating such registration or listing.

(oo) Sarbanes-Oxley Act. There is and has been no failure on the part of the Company or any of the Company's officers or directors, in their capacities as such, to comply with any provision of the Sarbanes-Oxley Act of 2002 and the rules and regulations promulgated in connection therewith (the "Sarbanes-Oxley Act") in any material respect, including Section 402 related to loans and Sections 302 and 906 related to certifications.

(pp) No Unlawful Payments. Neither the Company nor any of its subsidiaries, nor any director or officer of the Company or its subsidiaries, nor, to the Company's knowledge, any agent, employee or representative of the Company or its subsidiaries, affiliate or other person associated with or acting on behalf of the Company or its subsidiaries, has (i) used any corporate funds for any unlawful contribution, gift, entertainment or other unlawful expense relating to political activity; (ii) made or taken an act in furtherance of an offer, promise or authorization of any direct or indirect unlawful payment of corporate funds or benefit to any foreign or domestic government or regulatory official or employee, including, without limitation, of any government-owned or controlled entity or of a public international organization, or any person acting in an official capacity for or on behalf of any of the foregoing, or any political party or party official or candidate for political office; (iii) violated or is in violation of any provision of the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.K. Bribery Act 2010, or any applicable law or regulation implementing the OECD Convention on Combating Bribery of Foreign Public Officials in International Business Transactions, or committed an offense under any other applicable anti-bribery or anti-corruption laws; or (iv) made, offered, agreed, requested or taken an act in furtherance of any unlawful bribe or other unlawful benefit, including, without limitation, any rebate, payoff, influence payment, kickback or other unlawful or improper payment or benefit. The Company has instituted, maintained and enforced, and will continue to maintain and enforce policies and procedures designed to promote and ensure compliance with all applicable anti-bribery and anti-corruption laws.

(qq) Statistical and Market Data. The statistical and market related data included in the Registration Statement and the Prospectus are based on or derived from sources that the Company believes to be reliable and accurate, and such data agree with the sources from which they are derived.

(rr) Compliance with Anti-Money Laundering Laws. The operations of the Company and its subsidiaries are and have been conducted at all times in compliance with applicable financial recordkeeping and reporting requirements of the Currency and Foreign Transactions Reporting Act of 1970, as amended, those of the Bank Secrecy Act, as amended by Title III of the Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act of 2001 (USA PATRIOT Act), and the applicable money laundering statutes of all jurisdictions in which the Company and its subsidiaries conduct business, the rules and regulations thereunder and any related or similar rules, regulations or guidelines, issued, administered or enforced by any governmental or regulatory agency (collectively, the "**Anti-Money Laundering Laws**"), and no action, suit or proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company or any of its subsidiaries with respect to the Anti-Money Laundering Laws is pending, or to the Company's knowledge, threatened.

(ss) No Conflicts with Sanctions Laws. Neither the Company nor any of its subsidiaries, nor any director or officer of the Company or its subsidiaries, nor, to the Company's knowledge, any agent, employee or representative of the Company or its subsidiaries, affiliate or other person associated with or acting on behalf of the Company or its subsidiaries is currently the subject or target of any sanctions administered or enforced by the U.S. government (including, without limitation, the Office of Foreign Assets Control of the U.S. Treasury Department ("**OFAC**") or the U.S. Department of State and including, without limitation, the designation as a "specially designated national" or "blocked person"), the United Nations Security Council, the European Union, Her Majesty's Treasury or other relevant sanctions authority (collectively, "**Sanctions**"), nor is the Company or any of its subsidiaries located,

organized or resident in a country or territory that is the subject or the target of Sanctions, including, without limitation, Cuba, Iran, North Korea, Crimea and Syria (each, a “**Sanctioned Country**”); and the Company will not directly or indirectly use the proceeds of the offering of the Shares hereunder, or lend, contribute or otherwise make available such proceeds to any subsidiary, joint venture partner or other person or entity (i) to fund or facilitate any activities of or business with any person that, at the time of such funding or facilitation, is the subject or the target of Sanctions, (ii) to fund or facilitate any activities of or business in any Sanctioned Country or (iii) in any other manner that will result in a violation by any such person (including any person participating in the transaction, whether as underwriter, advisor, investor or otherwise) of Sanctions. Since inception, the Company and its subsidiaries have not knowingly engaged in, are not now knowingly engaged in, and will not engage in, any dealings or transactions with any person that at the time of the dealing or transaction is or was the subject or the target of Sanctions or with any Sanctioned Country.

(tt) No Associated Persons: FINRA Matters. Neither the Company nor, to the Company’s knowledge, any of its affiliates (within the meaning of FINRA Rule 5121(f)(1)) directly or indirectly controls, is controlled by, or is under common control with, or is an associated person (within the meaning of Article I, Section 1(ee) of the By-laws of FINRA) of, any member firm of FINRA.

(uu) No Integration. Except as described in the Registration Statement or the Prospectus, the Company has not sold, issued or distributed any Common Shares during the six-month period preceding the date hereof, including any sales pursuant to Rule 144A, or Regulation D or S of the Rules and Regulations, other than shares issued pursuant to employee benefit plans, qualified stock option plans or other employee compensation plans or pursuant to outstanding options, rights or warrants.

(vv) No Ratings. There are no securities or preferred stock of or guaranteed by the Company or any of its subsidiaries that are rated by a “nationally recognized statistical rating organization,” as such term is defined in Section 3(a)(62) of the Exchange Act.

(ww) eXtensible Business Reporting Language. The interactive data in eXtensible Business Reporting Language included or incorporated by reference in the Registration Statement fairly presents the information called for in all material respects and has been prepared in accordance with the Commission’s rules and guidelines applicable thereto.

(xx) Compliance with Applicable Laws. The Company and each of its Subsidiaries (A) to its knowledge, is and at all times has been in material compliance with all statutes, rules and regulations applicable to the ownership, testing, development, manufacture, packaging, processing, use, distribution, marketing, labeling, promotion, sale, offer for sale, storage, import, export or disposal of any product under development or manufactured by the Company or its Subsidiaries (“**Applicable Laws**”), (B) has not received any Form 483 from the FDA, notice of adverse finding, warning letter, or other written correspondence or notice from the FDA or any other federal, state, local or foreign governmental or regulatory authority alleging or asserting material noncompliance with any Applicable Laws or any licenses, certificates, approvals, clearances, authorizations, permits and supplements or amendments thereto required by any such Applicable Laws (“**Authorizations**”), which would, individually or in the aggregate, result in a

Material Adverse Effect; (C) possesses all material Authorizations and such Authorizations are valid and in full force and effect and the Company and each of its Subsidiaries are not in material violation of any term of any such Authorizations, except where any failure to possess, lack of validity or failure to be in full force and effect would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect; (D) has not received written notice of any claim, action, suit, proceeding, hearing, enforcement, investigation, arbitration or other action from the FDA or any other federal, state, local or foreign governmental or regulatory authority or third party alleging that any Company product, operation or activity is in material violation of any Applicable Laws or Authorizations and has no knowledge that the FDA or any other federal, state, local or foreign governmental or regulatory authority or third party is considering any such claim, litigation, arbitration, action, suit, investigation or proceeding against the Company or any of its Subsidiaries; (E) other than as described in the Registration Statement and the Prospectus, has not received notice that the FDA or any other federal, state, local or foreign governmental or regulatory authority has taken, is taking or intends to take action to limit, suspend, modify or revoke any material Authorizations that would reasonably be expected to have a Material Adverse Effect and has no knowledge that the FDA or any other federal, state, local or foreign governmental or regulatory authority is considering such action; and (F) to its knowledge, has filed, obtained, maintained or submitted all reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments as required by any Applicable Laws or Authorizations except where the failure to file such reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments would not reasonably be expected to result in a Material Adverse Effect, and that all such reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments were materially complete and correct on the date filed (or were corrected or supplemented by a subsequent submission).

(yy) Duties, Transfer Taxes, Etc. No stamp or other issuance or transfer taxes or duties and no capital gains, income, withholding or other taxes are payable by the Agent in the United States or any political subdivision or taxing authority thereof or therein in connection with the execution, delivery or performance of this Agreement by the Company or the sale and delivery by the Company of the Shares.

(zz) Data Privacy and Security Laws. The Company and its subsidiaries are, and during the past three years were, in material compliance with all applicable data privacy and security laws and regulations, including without limitation the Health Insurance Portability and Accountability Act of 1996 (“**HIPAA**”) (42 U.S.C. Section 1320d et seq.), as amended by the Health Information Technology for Economic and Clinical Health Act (the “**HITECH Act**”) (42 U.S.C. Section 17921 et seq.); and the Company and its subsidiaries have taken reasonable actions to prepare to comply with the European Union General Data Protection Regulation (“**GDPR**”) (EU 2016/679) and all other applicable data privacy and security laws and regulations that are effective as of the date hereof and for which any non-compliance with same would be reasonably likely to create a material liability (collectively, the “**Privacy Laws**”). To ensure compliance with the Privacy Laws, the Company and its subsidiaries have in place policies and procedures relating to data privacy and security and the collection, storage, use, disclosure, handling, and analysis of Personal Data (the “**Policies**”) and take appropriate steps reasonably designed to ensure compliance in all material respects with such Policies. During the past three years, where required by applicable Privacy Laws, the Company has provided accurate

notice of its externally facing Policies then in effect to its customers, employees, third-party vendors and representatives. Each of the Company's notices regarding the Company's Policies (i) provides accurate and sufficient notice of the Company's then-current privacy practices relating to its subject matter; and (ii) does not contain any material omissions of the Company's then-current privacy practices relating to its subject matter. "**Personal Data**" means: (i) any data or information under the applicable Privacy Laws related to an identifiable natural person alone or in combination with other data and information that can be used to identify a natural person as a natural person's name, street address, telephone number, e-mail address, social security number or tax identification number, driver's license number, passport number, credit card number, bank information, or customer or account number in connection with a password; (ii) any information which would qualify as "personally identifying information" under the Federal Trade Commission Act, as amended; (iii) Protected Health Information as defined by HIPAA; (iv) "personal data" as defined by GDPR; and (v) any other piece of information under applicable Privacy Laws that identifies such natural person, or his or her family, or identifies a specific person's health condition or sexual orientation. The Company further certifies that neither it nor any subsidiary: (i) has received notice of any actual or alleged violation of any of the Privacy Laws; or (ii) is a party to any order, decree, or settlement agreement that imposes any obligation or liability under any Privacy Law.

(aaa) Cybersecurity; Data Protection. To the Company's knowledge, the Company and its subsidiaries' information technology assets and equipment, computers, systems, networks, hardware, software, websites, applications, and databases (collectively, "**IT Systems**") are adequate for, and operate and perform in all material respects as required in connection with the operation of the business of the Company and its subsidiaries as currently conducted, free and clear of all material bugs, errors, defects, Trojan horses, time bombs, malware and other corruptants. The Company and its subsidiaries have at all times during the past three years implemented and maintained all reasonably necessary controls, policies, procedures, and safeguards to maintain and protect their confidential information and the integrity, continuous operation, redundancy and security of all IT Systems and data (including all Personal Data, sensitive, confidential or regulated data ("**Confidential Data**")) used in connection with their businesses, and, to the Company's knowledge, there have been no breaches, violations, outages or unauthorized uses of or accesses to same, except for those that have been remedied without material cost or liability or the duty to notify any other person.

Any certificate signed by any officer or representative of the Company or any of its subsidiaries and delivered to the Agent or counsel for the Agent in connection with an issuance of Shares shall be deemed a representation and warranty by the Company to the Agent as to the matters covered thereby on the date of such certificate.

The Company acknowledges that the Agent and, for purposes of the opinions to be delivered pursuant to Section 4(o) hereof, counsel to the Company and counsel to the Agent, will rely upon the accuracy and truthfulness of the foregoing representations and hereby consents to such reliance.

Section 3. ISSUANCE AND SALE OF COMMON SHARES

(a) Sale of Securities. On the basis of the representations, warranties and agreements herein contained, but subject to the terms and conditions herein set forth, the Company and the Agent agree that the Company may from time to time seek to sell Shares through the Agent, acting as sales agent, or directly to the Agent, acting as principal, as follows, with an aggregate Sales Price of up to the Maximum Program Amount, based on and in accordance with Issuance Notices as the Company may deliver, during the Agency Period.

(b) Mechanics of Issuances.

(i) Issuance Notice. Upon the terms and subject to the conditions set forth herein, on any Trading Day during the Agency Period on which the conditions set forth in Section 5(a) and Section 5(b) shall have been satisfied, the Company may exercise its right to request an issuance of Shares by delivering to the Agent an Issuance Notice; *provided, however*, that (A) in no event may the Company deliver an Issuance Notice to the extent that (I) the sum of (x) the aggregate Sales Price of the requested Issuance Amount, plus (y) the aggregate Sales Price of all Shares issued under all previous Issuance Notices effected pursuant to this Agreement, would exceed the Maximum Program Amount; and (B) prior to delivery of any Issuance Notice, the period set forth for any previous Issuance Notice shall have expired or been terminated. An Issuance Notice shall be considered delivered on the Trading Day that it is received by e-mail to the persons set forth in Schedule A hereto and confirmed by the Company by telephone (including a voicemail message to the persons so identified), with the understanding that, with adequate prior written notice, the Agent may modify the list of such persons from time to time.

(ii) Agent Efforts. Upon the terms and subject to the conditions set forth in this Agreement, upon the receipt of an Issuance Notice, the Agent will use its commercially reasonable efforts consistent with its normal sales and trading practices to place the Shares with respect to which the Agent has agreed to act as sales agent, subject to, and in accordance with the information specified in, the Issuance Notice, unless the sale of the Shares described therein has been suspended, cancelled or otherwise terminated in accordance with the terms of this Agreement. For the avoidance of doubt, the parties to this Agreement may modify an Issuance Notice at any time provided they both agree in writing to any such modification.

(iii) Method of Offer and Sale. The Shares may be offered and sold (A) in privately negotiated transactions with the consent of the Company; (B) as block transactions; or (C) by any other method permitted by law deemed to be an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act, including sales made directly on the Principal Market or sales made into any other existing trading market of the Common Shares. Nothing in this Agreement shall be deemed to require either party to agree to the method of offer and sale specified in the preceding sentence, and (except as specified in clauses (A) and (B) above) the method of placement of any Shares by the Agent shall be at the Agent's discretion.

(iv) Confirmation to the Company. If acting as sales agent hereunder, the Agent will provide written confirmation to the Company no later than the opening of the Trading Day next following the Trading Day on which it has placed Shares hereunder setting forth the number of shares sold on such Trading Day, the corresponding Sales Price and the Issuance Price payable to the Company in respect thereof.

(v) Settlement. Each issuance of Shares will be settled on the applicable Settlement Date for such issuance of Shares and, subject to the provisions of Section 5, on or before each Settlement Date, the Company will, or will cause its transfer agent to, electronically transfer the Shares being sold by crediting the Agent or its designee's account at The Depository Trust Company through its Deposit/Withdrawal At Custodian (DWAC) System, or by such other means of delivery as may be mutually agreed upon by the parties hereto and, upon receipt of such Shares, which in all cases shall be freely tradable, transferable, registered shares in good deliverable form, the Agent will deliver, by wire transfer of immediately available funds, the related Issuance Price in same day funds delivered to an account designated by the Company prior to the Settlement Date. The Company may sell Shares to the Agent as principal at a price agreed upon at each relevant time Shares are sold pursuant to this Agreement (each, a "**Time of Sale**").

(vi) Suspension or Termination of Sales. Consistent with standard market settlement practices, the Company or the Agent may, upon notice to the other party hereto in writing or by telephone (confirmed immediately by verifiable email), suspend any sale of Shares, and the period set forth in an Issuance Notice shall immediately terminate; *provided, however*, that (A) such suspension and termination shall not affect or impair either party's obligations with respect to any Shares placed or sold hereunder prior to the receipt of such notice; (B) if the Company suspends or terminates any sale of Shares after the Agent confirms such sale to the Company, the Company shall still be obligated to comply with Section 3(b)(v) with respect to such Shares; and (C) if the Company defaults in its obligation to deliver Shares on a Settlement Date, the Company agrees that it will hold the Agent harmless against any loss, claim, damage or expense (including, without limitation, penalties, interest and reasonable legal fees and expenses), as incurred, arising out of or in connection with such default by the Company. The parties hereto acknowledge and agree that, in performing its obligations under this Agreement, the Agent may borrow Common Shares from stock lenders in the event that the Company has not delivered Shares to settle sales as required by subsection (v) above, and may use the Shares to settle or close out such borrowings. The Company agrees that no such notice shall be effective against the Agent unless it is made to the persons identified in writing by the Agent pursuant to Section 3(b)(i).

(vii) No Guarantee of Placement, Etc. The Company acknowledges and agrees that (A) there can be no assurance that the Agent will be successful in placing Shares; (B) the Agent will incur no liability or obligation to the Company or any other Person if it does not sell Shares; and (C) the Agent shall be under no obligation to purchase Shares on a principal basis pursuant to this Agreement, except as otherwise specifically agreed by the Agent and the Company.

(viii) Material Non-Public Information. Notwithstanding any other provision of this Agreement, the Company and the Agent agree that the Company shall not deliver any Issuance Notice to the Agent, and the Agent shall not be obligated to place any Shares, during any period in which the Company is in possession of material non-public information.

(c) Fees. As compensation for services rendered, the Company shall pay to the Agent, on the applicable Settlement Date, the Selling Commission for the applicable Issuance Amount (including with respect to any suspended or terminated sale pursuant to Section 3(b)(vi)) by the Agent deducting the Selling Commission from the applicable Issuance Amount.

(d) Expenses. The Company agrees to pay all costs, fees and expenses incurred in connection with the performance of its obligations hereunder and in connection with the transactions contemplated hereby, including without limitation (i) all expenses incident to the issuance and delivery of the Shares (including all printing and engraving costs); (ii) all fees and expenses of the registrar and transfer agent of the Shares; (iii) all necessary issue, transfer and other stamp taxes in connection with the issuance and sale of the Shares; (iv) all fees and expenses of the Company's counsel, independent public or certified public accountants and other advisors; (v) all costs and expenses incurred in connection with the preparation, printing, filing, shipping and distribution of the Registration Statement (including financial statements, exhibits, schedules, consents and certificates of experts), the Prospectus, any Free Writing Prospectus (as defined below) prepared by or on behalf of, used by, or referred to by the Company, and all amendments and supplements thereto, and this Agreement; (vi) all filing fees, attorneys' fees and expenses incurred by the Company or the Agent in connection with qualifying or registering (or obtaining exemptions from the qualification or registration of) all or any part of the Shares for offer and sale under the state securities or blue sky laws or the provincial securities laws of Canada, and, if requested by the Agent, preparing and printing a "Blue Sky Survey" or memorandum and a "Canadian wrapper," and any supplements thereto, advising the Agent of such qualifications, registrations, determinations and exemptions; (vii) the reasonable fees and disbursements of the Agent's counsel, including the reasonable fees and expenses of counsel for the Agent in connection with, FINRA review, if any, and approval of the Agent's participation in the offering and distribution of the Shares; (viii) the filing fees incident to FINRA review, if any; (ix) the costs and expenses of the Company relating to investor presentations on any "road show" undertaken in connection with the marketing of the offering of the Shares, including, without limitation, expenses associated with the preparation or dissemination of any electronic road show, expenses associated with the production of road show slides and graphics, fees and expenses of any consultants engaged in connection with the road show presentations with the prior approval of the Company, travel and lodging expenses of the representatives, employees and officers of the Company and of the Agent and any such consultants, and the cost of any aircraft chartered in connection with the road show; and (x) the fees and expenses associated with listing the Shares on the Principal Market. The fees and disbursements of Agent's counsel pursuant to subsections (vi) and (vii) above shall not exceed \$50,000.

Section 4. ADDITIONAL COVENANTS

The Company covenants and agrees with the Agent as follows, in addition to any other covenants and agreements made elsewhere in this Agreement:

(a) Exchange Act Compliance. During the Agency Period, the Company shall (i) file, on a timely basis, with the Commission all reports and documents required to be filed under Section 13, 14 or 15 of the Exchange Act in the manner and within the time periods required by the Exchange Act; and (ii) either (A) include in its quarterly reports on Form 10-Q and its annual reports on Form 10-K, a summary detailing, for the relevant reporting period, (1) the number of

Shares sold through the Agent pursuant to this Agreement and (2) the net proceeds received by the Company from such sales or (B) prepare a prospectus supplement containing, or include in such other filing permitted by the Securities Act or Exchange Act (each an “**Interim Prospectus Supplement**”), such summary information and, at least once a quarter and subject to this Section 4, file such Interim Prospectus Supplement pursuant to Rule 424(b) under the Securities Act (and within the time periods required by Rule 424(b) and Rule 430B under the Securities Act)).

(b) Securities Act Compliance. After the date of this Agreement, the Company shall promptly advise the Agent in writing (i) of the receipt of any comments of, or requests for additional or supplemental information from, the Commission; (ii) of the time and date of any filing of any post-effective amendment to the Registration Statement, any Rule 462(b) Registration Statement or any amendment or supplement to the Prospectus, any Free Writing Prospectus; (iii) of the time and date that any post-effective amendment to the Registration Statement or any Rule 462(b) Registration Statement becomes effective; and (iv) of the issuance by the Commission of any stop order suspending the effectiveness of the Registration Statement or any post-effective amendment thereto, any Rule 462(b) Registration Statement or any amendment or supplement to the Prospectus or of any order preventing or suspending the use of any Free Writing Prospectus or the Prospectus, or of any proceedings to remove, suspend or terminate from listing or quotation the Common Shares from any securities exchange upon which they are listed for trading or included or designated for quotation, or of the threatening or initiation of any proceedings for any of such purposes. If the Commission shall enter any such stop order at any time, the Company will use its reasonable best efforts to obtain the lifting of such order as soon as practicable. Additionally, the Company agrees that it shall comply with the provisions of Rule 424(b) and Rule 433, as applicable, under the Securities Act and will use its reasonable efforts to confirm that any filings made by the Company under such Rule 424(b) or Rule 433 were received in a timely manner by the Commission.

(c) Amendments and Supplements to the Prospectus and Other Securities Act Matters. If any event shall occur or condition exist as a result of which it is necessary to amend or supplement the Prospectus so that the Prospectus does not include an untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances when the Prospectus is delivered to a purchaser, not misleading, or if in the opinion of the Agent or counsel for the Agent it is otherwise necessary to amend or supplement the Prospectus to comply with applicable law, including the Securities Act, the Company agrees (subject to Section 4(d) and 4(f)) to promptly prepare, file with the Commission and furnish at its own expense to the Agent, amendments or supplements to the Prospectus so that the statements in the Prospectus as so amended or supplemented will not include an untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances when the Prospectus is delivered to a purchaser, be misleading or so that the Prospectus, as amended or supplemented, will comply with applicable law including the Securities Act. Neither the Agent’s consent to, or delivery of, any such amendment or supplement shall constitute a waiver of any of the Company’s obligations under Sections 4(d) and 4(f). Notwithstanding the foregoing, the Company shall not be required to file such amendment or supplement if there is no pending Issuance Notice and the Company believes that it is in its best interests not to file such amendment or supplement.

(d) Agent's Review of Proposed Amendments and Supplements. During any period in which an Issuance Notice is pending, prior to amending or supplementing the Registration Statement (including any registration statement filed under Rule 462(b) under the Securities Act) or the Prospectus (excluding any amendment or supplement through incorporation of any report filed under the Exchange Act), the Company shall furnish to the Agent for review, a reasonable amount of time prior to the proposed time of filing or use thereof, a copy of each such proposed amendment or supplement, and the Company shall not file or use any such proposed amendment or supplement without the Agent's prior consent (not to be unreasonably withheld), and to file with the Commission within the applicable period specified in Rule 424(b) under the Securities Act any prospectus required to be filed pursuant to such Rule.

(e) Use of Free Writing Prospectus. Neither the Company nor the Agent has prepared, used, referred to or distributed, or will prepare, use, refer to or distribute, without the other party's prior written consent, any "written communication" that constitutes a "free writing prospectus" as such terms are defined in Rule 405 under the Securities Act with respect to the offering contemplated by this Agreement (any such free writing prospectus being referred to herein as a "**Free Writing Prospectus**").

(f) Free Writing Prospectuses. The Company shall furnish to the Agent for review, a reasonable amount of time prior to the proposed time of filing or use thereof, a copy of each proposed free writing prospectus or any amendment or supplement thereto to be prepared by or on behalf of, used by, or referred to by the Company and the Company shall not file, use or refer to any proposed free writing prospectus or any amendment or supplement thereto without the Agent's consent. The Company shall furnish to the Agent, without charge, as many copies of any free writing prospectus prepared by or on behalf of, or used by the Company, as the Agent may reasonably request. If at any time when a prospectus is required by the Securities Act (including, without limitation, pursuant to Rule 173(d)) to be delivered in connection with sales of the Shares (but in any event if at any time through and including the date of this Agreement) there occurred or occurs an event or development as a result of which any free writing prospectus prepared by or on behalf of, used by, or referred to by the Company conflicted or would conflict with the information contained in the Registration Statement or included or would include an untrue statement of a material fact or omitted or would omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances prevailing at that subsequent time, not misleading, the Company shall promptly amend or supplement such free writing prospectus to eliminate or correct such conflict or so that the statements in such free writing prospectus as so amended or supplemented will not include an untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances prevailing at such subsequent time, not misleading, as the case may be; *provided, however*, that prior to amending or supplementing any such free writing prospectus, the Company shall furnish to the Agent for review, a reasonable amount of time prior to the proposed time of filing or use thereof, a copy of such proposed amended or supplemented free writing prospectus and the Company shall not file, use or refer to any such amended or supplemented free writing prospectus without the Agent's consent.

(g) Filing of Agent Free Writing Prospectuses. The Company shall not take any action that would result in the Agent or the Company being required to file with the Commission pursuant to Rule 433(d) under the Securities Act a free writing prospectus prepared by or on behalf of the Agent that the Agent otherwise would not have been required to file thereunder.

(h) Copies of Registration Statement and Prospectus. After the date of this Agreement through the last time that a prospectus is required by the Securities Act (including, without limitation, pursuant to Rule 173(d)) to be delivered in connection with sales of the Shares, the Company agrees to furnish the Agent with copies (which may be electronic copies) of the Registration Statement and each amendment thereto, and with copies of the Prospectus and each amendment or supplement thereto in the form in which it is filed with the Commission pursuant to the Securities Act or Rule 424(b) under the Securities Act, both in such quantities as the Agent may reasonably request from time to time; and, if the delivery of a prospectus is required under the Securities Act or under the blue sky or securities laws of any jurisdiction at any time on or prior to the applicable Settlement Date for any period set forth in an Issuance Notice in connection with the offering or sale of the Shares and if at such time any event has occurred as a result of which the Prospectus as then amended or supplemented would include an untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made when such Prospectus is delivered, not misleading, or, if for any other reason it is necessary during such same period to amend or supplement the Prospectus or to file under the Exchange Act any document incorporated by reference in the Prospectus in order to comply with the Securities Act or the Exchange Act, to notify the Agent and to request that the Agent suspend offers to sell Shares (and, if so notified, the Agent shall cease such offers as soon as practicable); and if the Company decides to amend or supplement the Registration Statement or the Prospectus as then amended or supplemented, to advise the Agent promptly by telephone (with confirmation in writing) and to prepare and cause to be filed promptly with the Commission an amendment or supplement to the Registration Statement or the Prospectus as then amended or supplemented that will correct such statement or omission or effect such compliance; provided, however, that if during such same period the Agent is required to deliver a prospectus in respect of transactions in the Shares, the Company shall promptly prepare and file with the Commission such an amendment or supplement.

(i) Blue Sky Compliance. The Company shall cooperate with the Agent and counsel for the Agent to qualify or register the Shares for sale under (or obtain exemptions from the application of) the state securities or blue sky laws or Canadian provincial securities laws of those jurisdictions designated by the Agent, shall comply with such laws and shall continue such qualifications, registrations and exemptions in effect so long as required for the distribution of the Shares. The Company shall not be required to qualify as a foreign corporation or to take any action that would subject it to general service of process in any such jurisdiction where it is not presently qualified or where it would be subject to taxation as a foreign corporation. The Company will advise the Agent promptly of the suspension of the qualification or registration of (or any such exemption relating to) the Shares for offering, sale or trading in any jurisdiction or any initiation or threat of any proceeding for any such purpose, and in the event of the issuance of any order suspending such qualification, registration or exemption, the Company shall use its best efforts to obtain the withdrawal thereof as soon as practicable.

(j) Earnings Statement. As soon as practicable, the Company will make generally available to its security holders and to the Agent an earnings statement (which need not be audited) covering a period of at least twelve months beginning with the first fiscal quarter of the Company occurring after the date of this Agreement which shall satisfy the provisions of Section 11(a) of the Securities Act and Rule 158 under the Securities Act.

(k) Listing; Reservation of Shares. (a) The Company will maintain the listing of the Shares on the Principal Market; and (b) the Company will reserve and keep available at all times, free of preemptive rights, Shares for the purpose of enabling the Company to satisfy its obligations under this Agreement.

(l) Transfer Agent. The Company shall engage and maintain, at its expense, a registrar and transfer agent for the Shares.

(m) Due Diligence. During the term of this Agreement, the Company will reasonably cooperate with any reasonable due diligence review conducted by the Agent in connection with the transactions contemplated hereby, including, without limitation, providing information and making available documents and senior corporate officers, during normal business hours and at the Company's principal offices, as the Agent may reasonably request from time to time.

(n) Representations and Warranties. The Company acknowledges that each delivery of an Issuance Notice and each delivery of Shares on a Settlement Date shall be deemed to be (i) an affirmation to the Agent that the representations and warranties of the Company contained in or made pursuant to this Agreement are true and correct as of the date of such Issuance Notice or of such Settlement Date, as the case may be, as though made at and as of each such date, except as may be disclosed in the Prospectus (including any documents incorporated by reference therein and any supplements thereto); and (ii) an undertaking that the Company will advise the Agent if any of such representations and warranties will not be true and correct as of the Settlement Date for the Shares relating to such Issuance Notice, as though made at and as of each such date (except that such representations and warranties shall be deemed to relate to the Registration Statement and the Prospectus as amended and supplemented relating to such Shares).

(o) Deliverables at Triggering Event Dates; Certificates. The Company agrees that on or prior to the date of the first Issuance Notice and, during the term of this Agreement after the date of the first Issuance Notice, upon:

(A) the filing of the Prospectus or the amendment or supplement of any Registration Statement or Prospectus (other than a prospectus supplement relating solely to an offering of securities other than the Shares or a prospectus filed pursuant to Section 4(a)(ii)(B)), by means of a post-effective amendment, sticker or supplement, but not by means of incorporation of documents by reference into the Registration Statement or Prospectus;

(B) the filing with the Commission of an annual report on Form 10-K or a quarterly report on Form 10-Q (including any Form 10-K/A or Form 10-Q/A containing amended financial information or a material amendment to the previously filed annual report on Form 10-K or quarterly report on Form 10-Q), in each case, of the Company; or

(C) the filing with the Commission of a current report on Form 8-K of the Company containing amended financial information (other than information “furnished” pursuant to Item 2.02 or 7.01 of Form 8-K or to provide disclosure pursuant to Item 8.01 of Form 8-K relating to reclassification of certain properties as discontinued operations in accordance with Statement of Financial Accounting Standards No. 144) that is material to the offering of securities of the Company in the Agent’s reasonable discretion;

(any such event, a “**Triggering Event Date**”), the Company shall furnish the Agent (but in the case of clause (C) above only if the Agent reasonably determines that the information contained in such current report on Form 8-K of the Company is material) with a certificate as of the Triggering Event Date, in the form and substance satisfactory to the Agent and its counsel, substantially similar to the form previously provided to the Agent and its counsel, modified, as necessary, to relate to the Registration Statement and the Prospectus as amended or supplemented, (A) confirming that the representations and warranties of the Company contained in this Agreement are true and correct, (B) that the Company has performed all of its obligations hereunder to be performed on or prior to the date of such certificate and as to the matters set forth in Section 5(a)(i) hereof, and (C) containing any other certification that the Agent shall reasonably request. The requirement to provide a certificate under this Section 4(o) shall be waived for any Triggering Event Date occurring at a time when no Issuance Notice is pending or a suspension is in effect, which waiver shall continue until the earlier to occur of the date the Company delivers instructions for the sale of Shares hereunder (which for such calendar quarter shall be considered a Triggering Event Date) and the next occurring Triggering Event Date. Notwithstanding the foregoing, if the Company subsequently decides to sell Shares following a Triggering Event Date when a suspension was in effect and did not provide the Agent with a certificate under this Section 4(o), then before the Company delivers the instructions for the sale of Shares or the Agent sells any Shares pursuant to such instructions, the Company shall provide the Agent with a certificate in conformity with this Section 4(o) dated as of the date that the instructions for the sale of Shares are issued.

(p) Legal Opinions. On or prior to the date of the first Issuance Notice and within five (5) Trading Days of each Triggering Event Date with respect to which the Company is obligated to deliver a certificate pursuant to Section 4(o) for which no waiver is applicable and excluding the date of this Agreement, a negative assurances letter and the written legal opinion of Fenwick & West LLP, counsel to the Company, and Drinker Biddle & Reath LLP, intellectual property counsel to the Company, each dated the date of delivery, in form and substance reasonably satisfactory to Agent and its counsel, substantially similar to the form previously provided to the Agent and its counsel, modified, as necessary, to relate to the Registration Statement and the Prospectus as then amended or supplemented; provided, however, the Company shall be required to furnish no more than one opinion hereunder per calendar quarter. In lieu of such opinions for subsequent periodic filings, in the discretion of the Agent, the Company may furnish a reliance letter from such counsel to the Agent, permitting the Agent to rely on a previously delivered opinion letter, modified as appropriate for any passage of time or Triggering Event Date (except that statements in such prior opinion shall be deemed to relate to the Registration Statement and the Prospectus as amended or supplemented as of such Triggering Event Date).

(q) Comfort Letter. On or prior to the date of the first Issuance Notice and within five (5) Trading Days of each Triggering Event Date with respect to which the Company is obligated to deliver a certificate pursuant to Section 4(o) for which no waiver is applicable, the Company shall cause PricewaterhouseCoopers LLP, the independent registered public accounting firm who has audited the financial statements included or incorporated by reference in the Registration Statement, to furnish the Agent a comfort letter, dated the date of delivery, in form and substance reasonably satisfactory to the Agent and its counsel, substantially similar to the form previously provided to the Agent and its counsel; provided, however, that any such comfort letter will only be required on the Triggering Event Date specified to the extent that it contains financial statements filed with the Commission under the Exchange Act and incorporated or deemed to be incorporated by reference into a Prospectus. If requested by the Agent, the Company shall also cause a comfort letter to be furnished to the Agent within ten (10) Trading Days of the date of occurrence of any material transaction or event requiring the filing of a current report on Form 8-K containing material amended financial information of the Company, including the restatement of the Company's financial statements. The Company shall be required to furnish no more than one comfort letter hereunder per calendar quarter.

(r) Secretary's Certificate. On or prior to the date of the first Issuance Notice and within five (5) Trading Days of each Triggering Event Date, the Company shall furnish the Agent a certificate executed by the Secretary of the Company, signing in such capacity, dated the date of delivery (i) certifying that attached thereto are true and complete copies of the resolutions duly adopted by the Board of Directors of the Company authorizing the execution and delivery of this Agreement and the consummation of the transactions contemplated hereby (including, without limitation, the issuance of the Shares pursuant to this Agreement), which authorization shall be in full force and effect on and as of the date of such certificate, (ii) certifying and attesting to the office, incumbency, due authority and specimen signatures of each Person who executed this Agreement for or on behalf of the Company, and (iii) containing any other certification that the Agent shall reasonably request.

(s) Agent's Own Account; Clients' Account. The Company consents to the Agent trading, in compliance with applicable law, in the Common Shares for the Agent's own account and for the account of its clients at the same time as sales of the Shares occur pursuant to this Agreement.

(t) Investment Limitation. The Company shall not invest, or otherwise use the proceeds received by the Company from its sale of the Shares in such a manner as would require the Company or any of its subsidiaries to register as an investment company under the Investment Company Act.

(u) Market Activities. The Company will not take, directly or indirectly, any action designed to or that might be reasonably expected to cause or result in stabilization or manipulation of the price of the Shares or any other reference security, whether to facilitate the sale or resale of the Shares or otherwise, and the Company will, and shall cause each of its affiliates to, comply with all applicable provisions of Regulation M. If the limitations of Rule 102 of Regulation M ("**Rule 102**") do not apply with respect to the Shares or any other reference security pursuant to any exception set forth in Section (d) of Rule 102, then promptly upon notice from the Agent (or, if later, at the time stated in the notice), the Company will, and shall cause each of its affiliates to, comply with Rule 102 as though such exception were not available but the other provisions of Rule 102 (as interpreted by the Commission) did apply. The Company shall promptly notify the Agent if it no longer meets the requirements set forth in Section (d) of Rule 102.

(v) Notice of Other Sale. Without the written consent of the Agent, the Company will not, directly or indirectly, offer to sell, sell, contract to sell, grant any option to sell or otherwise dispose of any Common Shares or securities convertible into or exchangeable for Common Shares (other than Shares hereunder), warrants or any rights to purchase or acquire Common Shares, during the period beginning on the third Trading Day immediately prior to the date on which any Issuance Notice is delivered to the Agent hereunder and ending on the third Trading Day immediately following the Settlement Date with respect to Shares sold pursuant to such Issuance Notice; provided, however, that such restriction will not be required in connection with the Company's (i) issuance or sale of Common Shares, options to purchase Common Shares or Common Shares issuable upon the exercise of options or other equity awards pursuant to any employee or director share option, incentive or benefit plan, share purchase or ownership plan, long-term incentive plan, dividend reinvestment plan, inducement award under the Principal Market rules or other compensation plan of the Company or its subsidiaries, as in effect on the date of this Agreement, (ii) issuance or sale of Common Shares issuable upon exchange, conversion or redemption of securities or the exercise or vesting of warrants, options or other equity awards outstanding at the date of this Agreement, (iii) issuance or sale of Common Shares or securities convertible into or exchangeable for Common Shares as consideration for mergers, acquisitions, other business combinations, joint ventures or strategic alliances occurring after the date of this Agreement which are not used for capital raising purposes and (iv) modification of any outstanding options, warrants or any rights to purchase or acquire Common Shares.

Section 5. CONDITIONS TO DELIVERY OF ISSUANCE NOTICES AND TO SETTLEMENT

(a) Conditions Precedent to the Right of the Company to Deliver an Issuance Notice and the Obligation of the Agent to Sell Shares. The right of the Company to deliver an Issuance Notice hereunder is subject to the satisfaction, on the date of delivery of such Issuance Notice, and the obligation of the Agent to use its commercially reasonable efforts to place Shares during the applicable period set forth in the Issuance Notice is subject to the satisfaction, on each Trading Day during the applicable period set forth in the Issuance Notice, of each of the following conditions:

- (i) Accuracy of the Company's Representations and Warranties; Performance by the Company. The Company shall have delivered the certificate required to be delivered pursuant to Section 4(o) on or before the date on which delivery of such certificate is required pursuant to Section 4(o). The Company shall have performed, satisfied and complied with all covenants, agreements and conditions required by this Agreement to be performed, satisfied or complied with by the Company at or prior to such date, including, but not limited to, the covenants contained in Section 4(p), Section 4(q) and Section 4(r).

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- (ii) No Injunction. No statute, rule, regulation, executive order, decree, ruling or injunction shall have been enacted, entered, promulgated or endorsed by any court or governmental authority of competent jurisdiction or any self-regulatory organization having authority over the matters contemplated hereby that prohibits or directly and materially adversely affects any of the transactions contemplated by this Agreement, and no proceeding shall have been commenced that may have the effect of prohibiting or materially adversely affecting any of the transactions contemplated by this Agreement.
- (iii) Material Adverse Changes. Except as disclosed in the Prospectus and the Time of Sale Information, (a) in the judgment of the Agent there shall not have occurred any Material Adverse Change; and (b) there shall not have occurred any downgrading, nor shall any notice have been given of any intended or potential downgrading or of any review for a possible change that does not indicate the direction of the possible change, in the rating accorded any securities of the Company or any of its subsidiaries by any “nationally recognized statistical rating organization” as such term is defined for purposes of Section 3(a)(62) of the Exchange Act.
- (iv) No Suspension of Trading in or Delisting of Common Shares; Other Events. The trading of the Common Shares (including without limitation the Shares) shall not have been suspended by the Commission, the Principal Market or FINRA and the Common Shares (including without limitation the Shares) shall have been approved for listing or quotation on and shall not have been delisted from the the Nasdaq Stock Market, the New York Stock Exchange or any of their constituent markets. There shall not have occurred (and be continuing in the case of occurrences under clauses (i) and (ii) below) any of the following: (i) trading or quotation in any of the Company’s securities shall have been suspended or limited by the Commission or by the Principal Market or trading in securities generally on either the Principal Market shall have been suspended or limited, or minimum or maximum prices shall have been generally established on any of such stock exchanges by the Commission or the FINRA; (ii) a general banking moratorium shall have been declared by any of federal or New York, authorities; or (iii) there shall have occurred any outbreak or escalation of national or international hostilities or any crisis or calamity, or any change in the United States or international financial markets, or any substantial change or development involving a prospective substantial change in United States’ or international political, financial or economic conditions, as in the judgment of the Agent is material and adverse and makes it impracticable to market the Shares in the manner and on the terms described in the Prospectus or to enforce contracts for the sale of securities.

(b) Documents Required to be Delivered on each Issuance Notice Date. The Agent’s obligation to use its commercially reasonable efforts to place Shares hereunder shall additionally be conditioned upon the delivery to the Agent on or before the Issuance Notice Date of a certificate in form and substance reasonably satisfactory to the Agent, executed by the Chief Executive Officer, President or Chief Financial Officer of the Company, to the effect that all conditions to the delivery of such Issuance Notice shall have been satisfied as at the date of such certificate (which certificate shall not be required if the foregoing representations shall be set forth in the Issuance Notice).

(c) No Misstatement or Material Omission. Agent shall not have advised the Company that the Registration Statement, the Prospectus or the Time of Sale Information, or any amendment or supplement thereto, contains an untrue statement of fact that in the Agent's reasonable opinion is material, or omits to state a fact that in the Agent's reasonable opinion is material and is required to be stated therein or is necessary to make the statements therein not misleading.

Section 6. INDEMNIFICATION AND CONTRIBUTION

(a) Indemnification of the Agent. The Company agrees to indemnify and hold harmless the Agent, its officers and employees, and each person, if any, who controls the Agent within the meaning of the Securities Act or the Exchange Act against any loss, claim, damage, liability or expense, as incurred, to which the Agent or such officer, employee or controlling person may become subject, under the Securities Act, the Exchange Act, other federal or state statutory law or regulation, or the laws or regulations of foreign jurisdictions where Shares have been offered or sold or at common law or otherwise (including in settlement of any litigation), insofar as such loss, claim, damage, liability or expense (or actions in respect thereof as contemplated below) arises out of or is based upon (i) any untrue statement or alleged untrue statement of a material fact contained in the Registration Statement, or any amendment thereto, including any information deemed to be a part thereof pursuant to Rule 430B under the Securities Act, or the omission or alleged omission therefrom of a material fact required to be stated therein or necessary to make the statements therein not misleading; or (ii) any untrue statement or alleged untrue statement of a material fact contained in any Free Writing Prospectus that the Company has used, referred to or filed, or is required to file, pursuant to Rule 433(d) of the Securities Act or the Prospectus (or any amendment or supplement thereto), or the omission or alleged omission therefrom of a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading, and to reimburse the Agent and each such officer, employee and controlling person for any and all expenses (including the reasonable fees and disbursements of counsel chosen by the Agent) as such expenses are reasonably incurred by the Agent or such officer, employee or controlling person in connection with investigating, defending, settling, compromising or paying any such loss, claim, damage, liability, expense or action; provided, however, that the foregoing indemnity agreement shall not apply to any loss, claim, damage, liability or expense to the extent, but only to the extent, arising out of or based upon any untrue statement or alleged untrue statement or omission or alleged omission made in reliance upon and in conformity with written information furnished to the Company by the Agent expressly for use in the Registration Statement, any such Free Writing Prospectus or the Prospectus (or any amendment or supplement thereto), it being understood and agreed that the only such information furnished by the Agent to the Company consists of the information described in subsection (b) below. The indemnity agreement set forth in this Section 6(a) shall be in addition to any liabilities that the Company may otherwise have.

(b) Indemnification of the Company, its Directors and Officers. The Agent agrees to indemnify and hold harmless the Company, each of its directors, each of its officers who signed the Registration Statement and each person, if any, who controls the Company within the meaning of the Securities Act or the Exchange Act against any loss, claim, damage, liability or expense, as incurred, to which the Company or any such director, officer or controlling person may become subject, under the Securities Act, the Exchange Act, or other federal or state statutory law or regulation, or the laws or regulations of foreign jurisdictions where Shares have been offered or sold or at common law or otherwise (including in settlement of any litigation), arises out of or is based upon (i) any untrue statement or alleged untrue statement of a material fact contained in the Registration Statement, or any amendment thereto, including any information deemed to be a part thereof pursuant to Rule 430B under the Securities Act, or the omission or alleged omission therefrom of a material fact required to be stated therein or necessary to make the statements therein not misleading; or (ii) any untrue statement or alleged untrue statement of a material fact contained in any Free Writing Prospectus that the Company has used, referred to or filed, or is required to file, pursuant to Rule 433(d) of the Securities Act or the Prospectus (or any amendment or supplement thereto), or the omission or alleged omission therefrom of a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; but, for each of (i) and (ii) above, only to the extent arising out of or based upon any untrue statement or alleged untrue statement or omission or alleged omission made in reliance upon and in conformity with written information furnished to the Company by the Agent expressly for use in the Registration Statement, any such Free Writing Prospectus or the Prospectus (or any amendment or supplement thereto), it being understood and agreed that the only such information furnished by the Agent to the Company consists of the information set forth in the ninth paragraph under the caption "Plan of Distribution" in the Prospectus, and to reimburse the Company and each such director, officer and controlling person for any and all expenses (including the fees and disbursements of one counsel chosen by the Company) as such expenses are reasonably incurred by the Company or such officer, director or controlling person in connection with investigating, defending, settling, compromising or paying any such loss, claim, damage, liability, expense or action. The indemnity agreement set forth in this Section 6(b) shall be in addition to any liabilities that the Agent or the Company may otherwise have.

(c) Notifications and Other Indemnification Procedures. Promptly after receipt by an indemnified party under this Section 6 of notice of the commencement of any action, such indemnified party will, if a claim in respect thereof is to be made against an indemnifying party under this Section 6, notify the indemnifying party in writing of the commencement thereof, but the omission so to notify the indemnifying party will not relieve it from any liability which it may have to any indemnified party for contribution or otherwise than under the indemnity agreement contained in this Section 6 or to the extent it is not prejudiced as a proximate result of such failure. In case any such action is brought against any indemnified party and such indemnified party seeks or intends to seek indemnity from an indemnifying party, the indemnifying party will be entitled to participate in, and, to the extent that it shall elect, jointly with all other indemnifying parties similarly notified, by written notice delivered to the indemnified party promptly after receiving the aforesaid notice from such indemnified party, to assume the defense thereof with counsel reasonably satisfactory to such indemnified party; provided, however, if the defendants in any such action include both the indemnified party and the indemnifying party and the indemnified party shall have reasonably concluded that a conflict

may arise between the positions of the indemnifying party and the indemnified party in conducting the defense of any such action or that there may be legal defenses available to it and/or other indemnified parties which are different from or additional to those available to the indemnifying party, the indemnified party or parties shall have the right to select separate counsel to assume such legal defenses and to otherwise participate in the defense of such action on behalf of such indemnified party or parties. Upon receipt of notice from the indemnifying party to such indemnified party of such indemnifying party's election so to assume the defense of such action and approval by the indemnified party of counsel, the indemnifying party will not be liable to such indemnified party under this Section 6 for any legal or other expenses subsequently incurred by such indemnified party in connection with the defense thereof unless (i) the indemnified party shall have employed separate counsel in accordance with the proviso to the preceding sentence (it being understood, however, that the indemnifying party shall not be liable for the fees and expenses of more than one separate counsel (together with local counsel), representing the indemnified parties who are parties to such action), which counsel (together with any local counsel) for the indemnified parties shall be selected by the Agent (in the case of counsel for the indemnified parties referred to in Section 6(a) and (b) above), (ii) the indemnifying party shall not have employed counsel reasonably satisfactory to the indemnified party to represent the indemnified party within a reasonable time after notice of commencement of the action or (iii) the indemnifying party has authorized in writing the employment of counsel for the indemnified party at the expense of the indemnifying party, in each of which cases the fees and expenses of counsel shall be at the expense of the indemnifying party and shall be paid as they are incurred.

(d) Settlements. The indemnifying party under this Section 6 shall not be liable for any settlement of any proceeding effected without its written consent, but if settled with such consent or if there be a final judgment for the plaintiff, the indemnifying party agrees to indemnify the indemnified party against any loss, claim, damage, liability or expense by reason of such settlement or judgment. Notwithstanding the foregoing sentence, if at any time an indemnified party shall have requested an indemnifying party to reimburse the indemnified party for fees and expenses of counsel as contemplated by Section 6(c) hereof, the indemnifying party agrees that it shall be liable for any settlement of any proceeding effected without its written consent if (i) such settlement is entered into more than 30 days after receipt by such indemnifying party of the aforesaid request; and (ii) such indemnifying party shall not have reimbursed the indemnified party in accordance with such request prior to the date of such settlement. No indemnifying party shall, without the prior written consent of the indemnified party, effect any settlement, compromise or consent to the entry of judgment in any pending or threatened action, suit or proceeding in respect of which any indemnified party is or could have been a party and indemnity was or could have been sought hereunder by such indemnified party, unless such settlement, compromise or consent includes an unconditional release of such indemnified party from all liability on claims that are the subject matter of such action, suit or proceeding.

(e) Contribution. If the indemnification provided for in this Section 6 is for any reason held to be unavailable to or otherwise insufficient to hold harmless an indemnified party in respect of any losses, claims, damages, liabilities or expenses referred to therein, then each indemnifying party shall contribute to the aggregate amount paid or payable by such indemnified party, as incurred, as a result of any losses, claims, damages, liabilities or expenses referred to

therein (i) in such proportion as is appropriate to reflect the relative benefits received by the Company, on the one hand, and the Agent, on the other hand, from the offering of the Shares pursuant to this Agreement; or (ii) if the allocation provided by clause (i) above is not permitted by applicable law, in such proportion as is appropriate to reflect not only the relative benefits referred to in clause (i) above but also the relative fault of the Company, on the one hand, and the Agent, on the other hand, in connection with the statements or omissions which resulted in such losses, claims, damages, liabilities or expenses, as well as any other relevant equitable considerations. The relative benefits received by the Company, on the one hand, and the Agent, on the other hand, in connection with the offering of the Shares pursuant to this Agreement shall be deemed to be in the same respective proportions as the total gross proceeds from the offering of the Shares (before deducting expenses) received by the Company bear to the total commissions received by the Agent. The relative fault of the Company, on the one hand, and the Agent, on the other hand, shall be determined by reference to, among other things, whether any such untrue or alleged untrue statement of a material fact or omission or alleged omission to state a material fact relates to information supplied by the Company, on the one hand, or the Agent, on the other hand, and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission.

The amount paid or payable by a party as a result of the losses, claims, damages, liabilities and expenses referred to above shall be deemed to include, subject to the limitations set forth in Section 6(c), any legal or other fees or expenses reasonably incurred by such party in connection with investigating or defending any action or claim. The provisions set forth in Section 6(c) with respect to notice of commencement of any action shall apply if a claim for contribution is to be made under this Section 6(e); *provided, however*, that no additional notice shall be required with respect to any action for which notice has been given under Section 6(c) for purposes of indemnification.

The Company and the Agent agree that it would not be just and equitable if contribution pursuant to this Section 6(e) were determined by pro rata allocation or by any other method of allocation which does not take account of the equitable considerations referred to in this Section 6(e).

Notwithstanding the provisions of this Section 6(e), the Agent shall not be required to contribute any amount in excess of the Selling Commission received by the Agent in connection with the offering contemplated hereby. No person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) shall be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation. For purposes of this Section 6(e), each officer and employee of the Agent and each person, if any, who controls the Agent within the meaning of the Securities Act or the Exchange Act shall have the same rights to contribution as the Agent, and each director of the Company, each officer of the Company who signed the Registration Statement, and each person, if any, who controls the Company within the meaning of the Securities Act and the Exchange Act shall have the same rights to contribution as the Company.

Section 7. TERMINATION & SURVIVAL

(a) Term. Subject to the provisions of this Section 7, the term of this Agreement shall continue from the date of this Agreement until the end of the Agency Period, unless earlier terminated by the parties to this Agreement pursuant to this Section 7.

(b) Termination; Survival Following Termination.

- (i) Either party may terminate this Agreement prior to the end of the Agency Period, by giving written notice as required by this Agreement, upon one Trading Day's notice to the other party; provided that, (A) if the Company terminates this Agreement after the Agent confirms to the Company any sale of Shares, the Company shall remain obligated to comply with Section 3(b)(v) with respect to such Shares and (B) Section 2, Section 3(d), Section 6, Section 7 and Section 8 shall survive termination of this Agreement. If termination shall occur prior to the Settlement Date for any sale of Shares, such sale shall nevertheless settle in accordance with the terms of this Agreement.
- (ii) In addition to the survival provision of Section 7(b)(i), the respective indemnities, agreements, representations, warranties and other statements of the Company, of its officers and of the Agent set forth in or made pursuant to this Agreement will remain in full force and effect, regardless of any investigation made by or on behalf of the Agent or the Company or any of its or their partners, officers or directors or any controlling person, as the case may be, and, anything herein to the contrary notwithstanding, will survive delivery of and payment for the Shares sold hereunder and any termination of this Agreement.

Section 8. MISCELLANEOUS

(a) Press Releases and Disclosure. The Company may issue a press release describing the material terms of the transactions contemplated hereby as soon as practicable following the date of this Agreement, and may file with the Commission a Current Report on Form 8-K, with this Agreement attached as an exhibit thereto, describing the material terms of the transactions contemplated hereby, and the Company shall consult with the Agent prior to making such disclosures, and the parties hereto shall use all commercially reasonable efforts, acting in good faith, to agree upon a text for such disclosures that is reasonably satisfactory to all parties hereto. No party hereto shall issue thereafter any press release or like public statement (including, without limitation, any disclosure required in reports filed with the Commission pursuant to the Exchange Act) related to this Agreement or any of the transactions contemplated hereby without the prior written approval of the other party hereto, except as may be necessary or appropriate in the reasonable opinion of the party seeking to make disclosure to comply with the requirements of applicable law or stock exchange rules. If any such press release or like public statement is so required, the party making such disclosure shall consult with the other party prior to making such disclosure, and the parties shall use all commercially reasonable efforts, acting in good faith, to agree upon a text for such disclosure that is reasonably satisfactory to all parties hereto.

(b) No Advisory or Fiduciary Relationship. The Company acknowledges and agrees that (i) the transactions contemplated by this Agreement, including the determination of any fees, are arm's-length commercial transactions between the Company and the Agent, (ii) when acting as a principal under this Agreement, the Agent is and has been acting solely as a principal is not the agent or fiduciary of the Company, or its stockholders, creditors, employees or any other party, (iii) the Agent has not assumed nor will assume an advisory or fiduciary responsibility in favor of the Company with respect to the transactions contemplated hereby or the process leading thereto (irrespective of whether the Agent has advised or is currently advising the Company on other matters) and the Agent does not have any obligation to the Company with respect to the transactions contemplated hereby except the obligations expressly set forth in this Agreement, (iv) the Agent and its affiliates may be engaged in a broad range of transactions that involve interests that differ from those of the Company, and (v) the Agent has not provided any legal, accounting, regulatory or tax advice with respect to the transactions contemplated hereby and the Company has consulted its own legal, accounting, regulatory and tax advisors to the extent it deemed appropriate.

(c) Research Analyst Independence. The Company acknowledges that the Agent's research analysts and research departments are required to and should be independent from their respective investment banking divisions and are subject to certain regulations and internal policies, and as such the Agent's research analysts may hold views and make statements or investment recommendations and/or publish research reports with respect to the Company or the offering that differ from the views of their respective investment banking divisions. The Company understands that the Agent is a full service securities firm and as such from time to time, subject to applicable securities laws, may effect transactions for its own account or the account of its customers and hold long or short positions in debt or equity securities of the companies that may be the subject of the transactions contemplated by this Agreement.

(d) Notices. All communications hereunder shall be in writing and shall be mailed, hand delivered or telecopied and confirmed to the parties hereto as follows:

If to the Agent:

Jefferies LLC
520 Madison Avenue
New York, NY 10022
Facsimile: (646) 786-5719
Attention: General Counsel

with a copy (which shall not constitute notice) to:

Cooley LLP
1114 Avenue of the Americas
New York, NY 10036
Facsimile: (212) 479-6275
Attention: Daniel I. Goldberg, Esq.

If to the Company:

Aeglea BioTherapeutics, Inc.
901 S. MoPac Expressway
Barton Oaks Plaza One, Suite 250
Austin, TX
Facsimile: 512-872-5121
Attention: Chief Executive Officer

with a copy (which shall not constitute notice) to:

Fenwick & West LLP
555 California Street, 12th Floor
San Francisco, CA
Facsimile: 415-281-1350
Attention: Robert A. Freedman

Any party hereto may change the address for receipt of communications by giving written notice to the others in accordance with this Section 8(d).

(e) Successors. This Agreement will inure to the benefit of and be binding upon the parties hereto, and to the benefit of the employees, officers and directors and controlling persons referred to in Section 6, and in each case their respective successors, and no other person will have any right or obligation hereunder. The term "successors" shall not include any purchaser of the Shares as such from the Agent merely by reason of such purchase.

(f) Partial Unenforceability. The invalidity or unenforceability of any Article, Section, paragraph or provision of this Agreement shall not affect the validity or enforceability of any other Article, Section, paragraph or provision hereof. If any Article, Section, paragraph or provision of this Agreement is for any reason determined to be invalid or unenforceable, there shall be deemed to be made such minor changes (and only such minor changes) as are necessary to make it valid and enforceable.

(g) Governing Law Provisions. This Agreement shall be governed by and construed in accordance with the internal laws of the State of New York applicable to agreements made and to be performed in such state. Any legal suit, action or proceeding arising out of or based upon this Agreement or the transactions contemplated hereby ("**Related Proceedings**") may be instituted in the federal courts of the United States of America located in the Borough of Manhattan in the City of New York or the courts of the State of New York in each case located in the Borough of Manhattan in the City of New York (collectively, the "**Specified Courts**"), and each party irrevocably submits to the exclusive jurisdiction (except for proceedings instituted in regard to the enforcement of a judgment of any such court (a "**Related Judgment**"), as to which such jurisdiction is non-exclusive) of such courts in any such suit, action or proceeding. Service of any process, summons, notice or document by mail to such party's address set forth above shall be effective service of process for any suit, action or other proceeding brought in any such court. The parties irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the Specified Courts and irrevocably and unconditionally waive and agree not to plead or claim in any such court that any such suit, action or other proceeding brought in any such court has been brought in an inconvenient forum.

(h) General Provisions. This Agreement constitutes the entire agreement of the parties to this Agreement and supersedes all prior written or oral and all contemporaneous oral agreements, understandings and negotiations with respect to the subject matter hereof. This Agreement may be executed in two or more counterparts, each one of which shall be an original, with the same effect as if the signatures thereto and hereto were upon the same instrument, and may be delivered by facsimile transmission or by electronic delivery of a portable document format (PDF) file. This Agreement may not be amended or modified unless in writing by all of the parties hereto, and no condition herein (express or implied) may be waived unless waived in writing by each party whom the condition is meant to benefit. The Article and Section headings herein are for the convenience of the parties only and shall not affect the construction or interpretation of this Agreement.

[Signature Page Immediately Follows]

If the foregoing is in accordance with your understanding of our agreement, kindly sign and return to the Company the enclosed copies hereof, whereupon this instrument, along with all counterparts hereof, shall become a binding agreement in accordance with its terms

Very truly yours,

AEGLEA BIOTHERAPEUTICS, INC.

By: /s/ Charles N. York II

Name: Charles N. York II

Title: Chief Financial Officer

The foregoing Agreement is hereby confirmed and accepted by the Agent in New York, New York as of the date first above written.

JEFFERIES LLC

By: /s/ Matthew Kim

Name: Matthew Kim

Title: Managing Director

EXHIBIT A

ISSUANCE NOTICE

[Date]

Jefferies LLC
520 Madison Avenue
New York, New York 10022

Attn: [_____]

Reference is made to the Open Market Sale Agreement between Aeglea BioTherapeutics, Inc. (the “**Company**”) and Jefferies LLC (the “**Agent**”) dated as of December 21, 2018. The Company confirms that all conditions to the delivery of this Issuance Notice are satisfied as of the date hereof.

Date of Delivery of Issuance Notice (determined pursuant to Section 3(b)(i)): _____

Issuance Amount (equal to the total Sales Price for such Shares):

\$ _____

Number of days in selling period: _____

First date of selling period: _____

Last date of selling period: _____

Settlement Date(s) if other than standard T+2 settlement:

Floor Price Limitation (in no event less than \$1.00 without the prior written consent of the Agent, which consent may be withheld in the Agent’s sole discretion): \$ ____ per share

Comments: _____

By: _____
Name:
Title:

Schedule A

Notice Parties

The Company

Anthony G. Quinn

Charles N. York II

The Agent

Michael Magarro

Donald Lynaugh

Matthew Kim

FORM OF DEBT SECURITY

[Face of Security]

AEGLEA BIOTHERAPEUTICS, INC.

[If applicable, insert—FOR PURPOSES OF THE ORIGINAL ISSUE DISCOUNT PROVISIONS OF THE INTERNAL REVENUE CODE OF 1986, THE ISSUE PRICE OF THIS SECURITY IS % OF ITS PRINCIPAL AMOUNT AT STATED MATURITY SET FORTH BELOW (ITS “PRINCIPAL AMOUNT”), THE AMOUNT OF ORIGINAL ISSUE DISCOUNT IS % OF ITS PRINCIPAL AMOUNT, THE YIELD TO MATURITY IS % AND THE ISSUE DATE IS]

[IF THE SECURITY IS A GLOBAL SECURITY, INSERT—THIS NOTE IS A GLOBAL SECURITY. IT IS EXCHANGEABLE FOR NOTES REGISTERED IN THE NAME OF A PERSON OTHER THAN THE DEPOSITARY (AS HEREINAFTER DEFINED) OR ITS NOMINEE ONLY IN THE LIMITED CIRCUMSTANCES HEREINAFTER DESCRIBED AND MAY NOT BE TRANSFERRED EXCEPT AS A WHOLE BY THE DEPOSITARY TO A NOMINEE OF THE DEPOSITARY OR BY A NOMINEE OF THE DEPOSITARY TO THE DEPOSITARY OR ANOTHER NOMINEE OF THE DEPOSITARY OR BY THE DEPOSITARY OR A NOMINEE OF THE DEPOSITARY TO A SUCCESSOR OF THE DEPOSITARY OR A NOMINEE OF SUCH SUCCESSOR DEPOSITARY.]

No.

\$
CUSIP No.

Aeglea BioTherapeutics, Inc., a Delaware Corporation (herein called the “Company”, which term includes any successor corporation under the Indenture referred to on the reverse hereof), for value received, hereby promises to pay to, or registered assigns, the principal sum of Dollars on [if Security is to bear interest prior to maturity, insert—, and to pay interest thereon from or from the most recent Interest Payment Date to which interest has been paid or duly provided for, semi-annually on and in each year, commencing , at the rate of % per annum, until the principal hereof is paid or made available for payment [if applicable, insert—, provided that any principal and premium, and any such installment of interest, which is overdue shall bear interest at the rate of % per annum (to the extent that the payment of such interest shall be legally enforceable), from the dates such amounts are due until they are paid or made available for payment, and such interest shall be payable on demand]. The interest so payable, and punctually paid or duly provided for, on any Interest Payment Date will, as provided in such Indenture, be paid to the Person in whose name this Security (or one or more Predecessor Securities) is registered at the close of business on the Record Date for such interest, which shall be the or (whether or not a Business Day), as the case may be, next preceding such Interest Payment Date. Any such interest not so punctually paid or duly provided for will forthwith cease to be payable to the Holder on such Record Date and may either be paid to the Person this Security (or one or more Predecessor Securities) is registered at the close of business on a Special Record Date for the payment of such Defaulted Interest to be fixed by the Trustee, notice whereof shall be given to Holders of Securities of this series not less than 10 days prior to such Special Record Date, or be paid at any time in any other lawful manner not inconsistent with the requirements of any securities exchange on which the Securities of this series may be listed, and upon such notice as may be required by such exchange, all as more fully provided in said Indenture. [If the Security is not to bear interest prior to maturity, insert—The principal of this Security shall not bear interest except in the case of a default in payment of principal upon acceleration, upon redemption or at Stated Maturity and in such case the overdue principal and any overdue premium shall bear interest at the rate of % per annum (to the extent that the payment of such interest shall be legally enforceable), from the dates such amounts are due until they are paid or made available for payment. Interest on any overdue principal or premium shall be payable on demand. [Any such interest on overdue principal or premium which is not paid on demand shall bear interest at the rate of % per annum (to the extent that the payment of such interest on interest shall be legally enforceable), from the date of such demand until the amount so demanded is paid or made available for payment. Interest on any overdue interest shall be payable on demand.]].

Payment of the principal of (and premium, if any, on) and [any such] interest on this Security will be made at the office or agency of the Company maintained for that purpose in in such coin or currency of [the United States of America] as at the time of payment is legal tender for payment of public and private debts; provided, however, that at the option of the Company payment of interest may be made by check mailed to the address of the Person entitled thereto as such address shall appear in the Register].

Reference is hereby made to the further provisions of this Security set forth on the reverse hereof, which further provisions shall for all purposes have the same effect as if set forth at this place.

Unless the certificate of authentication hereon has been manually executed by or on behalf of the Trustee under the Indenture referred to on the reverse hereof, this Security shall not be entitled to any benefit under the Indenture or be valid or obligatory for any purpose.

IN WITNESS WHEREOF, the Company has caused this instrument to be duly executed under its corporate seal.

Dated:

Aeglea BioTherapeutics, Inc.

By

_____ [Title]

Attest and Countersign

Secretary

[Reverse of Security.]

AEGLEA BIOTHERAPEUTICS, INC.

This Security is one of a duly authorized issue of securities of the Company (herein called the "Securities"), issued and to be issued in one or more series under an Indenture dated as of _____, (herein called the "Indenture," which term shall have the meaning assigned to it in such instrument), between the Company and _____, as trustee (herein called the "Trustee", which term includes any successor trustee under the Indenture), to which Indenture and all indentures supplemental thereto reference is hereby made for a statement of the respective rights, limitations or rights, duties and immunities thereunder of the Company, the Trustee and the Holders of the Securities and of the terms upon which the Securities are, and are to be, authenticated and delivered. This Security is one of the series designated on the face hereof[, limited in aggregate principal amount to \$ _____].

[If the Security is to be subordinated, insert—The indebtedness evidenced by this Security is, to the extent and in the manner set forth in the Indenture, expressly subordinated and subject in right of payment to the prior payment in full of all Senior Indebtedness (as defined in the Indenture) of the Company. This Security is issued subject to such provisions of the Indenture, and each Holder of this Security, by accepting the same, agrees to and shall be bound by such provisions and authorizes and directs the Trustee on the Holder's behalf to take such action as may be necessary or appropriate to acknowledge or effectuate such subordination as provided in the Indenture and appoints the Trustee such Holder's attorney-in-fact for any and all such purposes.]

The Securities of this series are subject to redemption upon not less than 30 days', and no more than 60 days, notice provided in the manner set forth in the Indenture, [(1) on in any year commencing with the year and ending with the year at the Redemption Price equal to 100% of the principal amount, and (2)] at any time [on or after], as a whole or in part, at the election of the principal the following Redemption Prices (expressed as percentages of the principal amount): If redeemed [on or before _____, _____%, and if redeemed] during the 12-month period beginning of the years indicated,

<u>Year</u>	<u>Redemption Price</u>	<u>Year</u>	<u>Redemption Price</u>

and thereafter at a Redemption Price equal to % of the principal amount together in the case of any such redemption with accrued interest to the Redemption Date, but interest installments whose Stated Maturity is on or prior to such Redemption Date will be payable to the Holders of such Securities of record at the close of business on the relevant record dates referred to on the face hereof, all as provided in the Indenture.

[If the Security is to be redeemable in part, insert—In the event of redemption of this Security in part only, a new Security or Securities of this series for the unredeemed portion hereof will be issued in the name of the Holder hereof upon the cancellation hereof.]

[If the Security is to be subject to repayment at the option of the Holder, insert—To be repaid at the option of the Holder, the Company must receive this Security, with the form of "Option to Elect Repayment" hereon duly completed, at an office or agency of the Company maintained for that purpose in (or at such other place of which the Company shall from time to time notify the Holder of this Security) not less than nor more than days prior to the Repayment Date. The exercise of the repayment option by the Holder shall be irrevocable.]

[If the Security is not to be subject to redemption at the option of the Company, insert—The Securities are not redeemable at the option of the Company prior to Maturity.]

[If the Security is not to be an Original Issue Discount Security, insert—If an Event of Default with respect to Securities of this series shall occur and be continuing, the principal of the Securities of this series may be declared due and payable in the manner and with the effect provided in the Indenture.]

The Indenture permits, with certain exceptions as therein provided, the amendment thereof and the modification of the rights and obligations of the Company and the rights of the Holders of the Securities of each series under the Indenture to be affected at any time by the Company with the consent of the Holders of not less than a majority in aggregate principal amount of the Securities at the time Outstanding of each series to be affected. The

Indenture also contains provisions permitting the Holders of a majority in principal amount of the Securities of each series at the time Outstanding, on behalf of the Holders of all Securities of such series, to waive compliance by the Company with certain provisions of the Indenture and certain past defaults under the Indenture and their consequences. Any such consent or waiver by the

Holder of this Security shall be conclusive and binding upon such Holder and upon all future Holders of this Security and of any Security issued upon the registration of transfer hereof or in exchange herefor or in lieu hereof, whether or not notation of such consent of waiver is made upon this Security.

As provided in and subject to the provisions of the indenture, the Holder of this Security shall not have the right to institute any proceeding with respect to the Indenture or for the appointment of a receiver or trustee or for any other remedy thereunder, unless such Holder shall have previously given the Trustee written notice of a continuing Event of Default with respect to the Securities of this series, the Holders of not less than 25% in principal amount of the Securities of this series at the time Outstanding shall have made written request to the trustee to institute proceedings in respect of such Event of Default as Trustee and offered the Trustee reasonable indemnity satisfactory to it, and the Trustee shall not have received from the Holders of a majority in principal amount of Securities of this series at the time Outstanding a direction inconsistent with such request, and shall have failed to institute any such proceeding, for 60 days after receipt of such notice, request and offer of indemnity. The foregoing shall not apply to any suit instituted by the Holder of this Security for the enforcement of any payment of principal hereof or any premium or interest hereon on or after the respective due dates expressed herein.

No reference herein to the Indenture and no provision of this Security or of the Indenture shall alter or impair the obligation of the Company, which is absolute and unconditional, to pay the principal of (and premium, if any, on) and interest on this Security at the times, place and rate, and in the coin or currency, herein prescribed.

[If the Security is to be in registered form, insert—As provided in the Indenture and subject to certain limitations therein set forth, the transfer of this Security is registrable in the Register, upon surrender of this Security for registration of transfer at the office or agency of the Company in any place where the principal of (and premium, if any, on) and interest on this Security are payable, duly endorsed by, or accompanied by a written instrument of transfer in form satisfactory to the Company and the Registrar duly executed by, the Holder hereof or his attorney duly authorized in writing, and, thereupon one or more new Securities of this series, of authorized denominations and for the same aggregate principal amount, will be issued to the designated transferee or transferees.]

[The Securities of this series are issuable only in registered form in denominations of \$ [and any integral multiple] [or increments of \$ in excess] thereof. As provided in the Indenture and subject to certain limitations therein set forth, Securities of this series are exchangeable for a like aggregate principal amount of Securities of this series of a different authorized denomination, as requested by the Holder surrendering the same.]

[No service charge shall be made for any such registration of transfer or exchange, but the Company may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection therewith.]

[Prior to due presentment of this Security for registration of transfer, the Company, the Trustee and any agent of the Company or the Trustee may treat the Person in whose name this Security is registered as the owner hereof for all purposes, whether or not this Security be overdue, and neither the Company, the Trustee nor any such agent shall be affected by notice to the contrary.]

[If the Security is a Global Security, insert—“Global Security” and “Global Securities” means a Security or Securities evidencing all or a part of a series of Securities, issued to the Depository (as hereinafter defined) for such Series or its nominee, and registered in the name of such Depository or its nominee. “Depository” means, with respect to the Securities of any series issuable or issued in whole or in part in the form of one or more Global Securities, the person designated as the Depository by the Company.]

No holder of any beneficial interest in this Security held on its behalf by a Depository or a nominee of such Depository shall have any rights under the Indenture with respect to such Global Security, and such Depository or nominee may be treated by the Company, the Trustee, and any agent of the Company or the Trustee as the owner of such Global Security for all purposes whatsoever. Notwithstanding the foregoing, nothing herein shall impair, as between a Depository and such holders of beneficial interests, the operation of customary practices governing the exercise of the rights of the Depository as Holder of any Security.

This Security is exchangeable, in whole but not in part, for Securities registered in the names of Persons other than the Depository or its nominee or in the name of a successor to the Depository or a nominee of such successor depository only if (i) the Depository notifies the Company that it is unwilling or unable to continue as Depository for

this Note or if at any time such Depository ceases to be a clearing agency registered under the Securities Exchange Act of 1934, as amended, and, in either case, a successor depository is not appointed by the Company within 90 days, (ii) the Company in its discretion at any time determines not to have all of the Securities of this series represented by one or more Global Security or Securities and notifies the Trustee thereof, or (iii) an Event of Default has occurred and is continuing with respect to the Securities of this series. If this Security is exchangeable pursuant to the preceding sentence, it shall be exchangeable for Securities issuable in authorized denominations and registered in such names as the Depository holding this Security shall direct. Subject to the foregoing, this Security is not exchangeable, except for a Security or Securities of the same aggregate denominations to be registered in the name of such Depository or its nominee or in the name of a successor to the Depository or a nominee of such successor depository.]

[The Indenture entitles Holders to receive annual reports with respect to the Trustee's eligibility and qualifications to serve as Trustee by filing their names and addresses with the Trustee for that purpose within two years preceding and mailing of any such annual report.]

No recourse shall be had for the payment of the principal of (and premium, if any, on) or interest on this Security, or for any claim based hereon, or otherwise in respect hereof, or based on or in respect of the Indenture of any indenture supplemental thereto, against any incorporator, stockholder, officer or director, as such, past, present or future, of the Company or any successor corporation, whether by virtue of any constitution, statute or rule of law, or by the enforcement of any assessment or penalty or otherwise, all such liability being, by the acceptance hereof and as part of the consideration for the issue hereof, expressly waived and released.

All terms used in this Security which are defined in the Indenture shall have the meanings assigned to them in the Indenture.

This Security, including without limitation the obligation of the Company contained herein to pay the principal of (and premium, if any, on) and interest on this Security in accordance with the terms hereof and of the Indenture, shall be construed in accordance with and governed by the laws of the State of New York.

[Trustee's Certificate of Authentication.]

This is one of the Securities of the series designated herein referred to in the within-mentioned Indenture.

_____, as
[Authenticating Agent for] the Trustee

By _____
Authorized Officer

AEGLEA BIOTHERAPEUTICS, INC.

And

, as Trustee

INDENTURE

Dated as of _____ ,

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CROSS-REFERENCE TABLE

<u>TIA SECTION</u>	<u>INDENTURE SECTION</u>
310(a)(1)(2)(5)	7.10
310(a)(3)(4)	Inapplicable
310(b)	7.8; 7.10
310(c)	Inapplicable
311(a)(b)	7.11
311(c)	Inapplicable
312(a)	2.6
312(b)(c)	10.3
313(a)(b)	7.6
313(c)	7.6; 10.2
313(d)	7.6
314(a)	4.2; 4.4; 10.2
314(b)	N/A
314(c)(1)(2)	10.4; 10.5
314(c)(3)	Inapplicable
314(d)	Inapplicable
314(e)	10.5

314(f)	Inapplicable
315(a)	7.1, 7.2
315(b)	7.5; 10.2
315(c)	7.1
315(d)	7.1; 7.2
315(e)	6.11
316(a)(last sentence)	2.10
316(a)(1)(A)	6.5
316(a)(1)(B)	6.4
316(a)(2)	8.2
316(b)	6.7
316(c)	8.4
317(a)(1)	6.8
317(a)(2)	6.9
317(b)	2.5; 7.12
318(a)	10.1

Note: This Cross-Reference Table shall not, for any purpose, be deemed to be a part of the Indenture.

INDENTURE, dated as of _____, _____, by and between Aeglea BioTherapeutics, Inc., a Delaware corporation, as Issuer (the “Company”) and _____, a _____ organized under the laws of _____, as Trustee (the “Trustee”).

RECITALS OF THE COMPANY

The Company has duly authorized the execution and delivery of this Indenture to provide for the issuance from time to time of its debentures, notes or other evidences of indebtedness to be issued in one or more series (the “Securities”), as herein provided, up to such principal amount as may from time to time be authorized in or pursuant to one or more resolutions of the Board of Directors or by supplemental indenture.

All things necessary to make this Indenture a valid agreement of the Company in accordance with its terms have been done, and the execution and delivery thereof have been in all respects duly authorized by the parties hereto.

NOW, THEREFORE, THIS INDENTURE WITNESSETH:

For and in consideration of the premises and the purchase of the Securities by the Holders thereof, it is mutually agreed, for the equal and proportionate benefit of all Holders of the Securities of a Series thereof, as follows:

ARTICLE 1 – DEFINITIONS AND INCORPORATION BY REFERENCE

1.1 DEFINITIONS.

“Affiliate” of any specified Person means any other Person which, directly or indirectly through one or more intermediaries, controls, or is controlled by or is under common control with, such specified Person. For the purposes of this definition, “control” (including, with correlative meanings, the terms “controlling,” “controlled by” and “under common control with”), as used with respect to any Person, means the possession, directly or indirectly, of the power to direct or cause the direction of the management or policies of such Person, whether through the ownership of voting securities, by agreement or otherwise.

“Agent” means any Registrar, Paying Agent, co-registrar or agent for service of notices and demands.

“Board of Directors” means the Board of Directors of the Company or any committee duly authorized to act therefor.

“Board Resolution” means a copy of a resolution certified pursuant to an Officers’ Certificate to have been duly adopted by the Board of Directors of the Company and to be in full force and effect on the date of such certification which has been delivered to the Trustee.

“Capital Stock” means, with respect to any Person, any and all shares or other equivalents (however designated) of capital stock, partnership interests or any other participation, right or other interest in the nature of an equity interest in such Person or any option, warrant or other security convertible into any of the foregoing.

“Company” means the party named as such in the first paragraph of this Indenture until a successor replaces such party pursuant to Article 5 of this Indenture, and thereafter means the successor and any other primary obligor on the Securities.

“Company Order” means a written order signed in the name of the Company by two Officers, one of whom must be its Chief Executive Officer or its Vice President of Finance.

“Company Request” means any written request signed in the name of the Company by its Chief Executive Officer, its President, any Vice President, its Chief Financial Officer or its Treasurer and attested to by its Secretary or any Assistant Secretary.

“Corporate Trust Office” means the office of the Trustee at which at any particular time its corporate trust business shall be principally administered.

“Default” means any event that is, or that with the passing of time or giving of notice or both would be, an Event of Default.

“Depository” means, with respect to the Securities of any Series issuable or issued in whole or in part in the form of one or more Global Securities, the Person designated as Depository for such Series by the Company, which Depository shall be a clearing agency registered under the Exchange Act, until a successor Depository shall have become such pursuant to the applicable provisions of this Indenture, and thereafter “Depository” shall mean each Person who is then a Depository hereunder, and if at any time there is more than one such Person, such Persons.

“Dollars” means the currency of the United States of America.

“Euro” means the single currency of participating member states of the economic and monetary union as contemplated in the Treaty on European Union.

“Exchange Act” means the Securities Exchange Act of 1934, as amended.

“Foreign Currency” means any currency or currency unit issued by a government other than the government of the United States of America.

“Foreign Government Obligations” means, with respect to Securities that are denominated in a Foreign Currency, (i) 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 (ii) obligations of a Person controlled or supervised by, or acting as an agency or instrumentality of, such government, the timely payment of which is unconditionally guaranteed as a full faith and credit obligation by such government, which, in either case under clauses (i) and (ii), are not callable or redeemable at the option of the issuer thereof.

“GAAP” means generally accepted accounting principles consistently applied as in effect in the United States of America from time to time.

“Global Security” or “Global Securities” means a Security or Securities, as the case may be, in the form established pursuant to Section 2.2, evidencing all or part of a Series of Securities issued to the Depository for such Series or its nominee, and registered in the name of such Depository or nominee, and bearing the legend set forth in Section 2.15(c) (or such other legend(s) as may be applied to such Securities in accordance with Section 2.2(24)).

“Holder” or “Securityholder” means the Person in whose name a Security is registered on the Registrar’s books.

“Indebtedness” means (without duplication), with respect to any Person, any indebtedness at any time outstanding, secured or unsecured, contingent or otherwise, which is for borrowed money (whether or not the recourse of the lender is to the whole of the assets of such Person or only to a portion thereof), or evidenced by bonds, notes, debentures or similar instruments, or representing the balance deferred and unpaid of the purchase price of any property (excluding any balances that constitute accounts payable or trade payables, and other accrued liabilities arising in the ordinary course of business), if and to the extent any of the foregoing indebtedness would appear as a liability upon a balance sheet of such Person prepared in accordance with GAAP.

“Indenture” means this Indenture as amended, restated or supplemented from time to time.

“Interest Payment Date,” when used with respect to any Security, means the Stated Maturity of an installment of interest on such Security.

“Lien” means, with respect to any property or assets of any Person, any mortgage or deed of trust, pledge, hypothecation, assignment, deposit arrangement, security interest, lien, charge, easement, encumbrance, preference, priority or other security agreement or preferential arrangement of any kind or nature whatsoever on or with respect to such property or assets (including, without limitation, any capitalized lease obligation, conditional sales or other title retention agreement having substantially the same economic effect as any of the foregoing).

“Maturity,” when used with respect to any Security, means the date on which the principal of such Security, or an installment of principal, becomes due and payable as therein or herein provided, whether at the Stated Maturity or by declaration of acceleration, call for redemption, notice of option to elect payment or otherwise.

“Officer” means the Chief Executive Officer, the President, any Vice President, the Chief Financial Officer, the Treasurer or the Secretary of the Company, or any other officer designated by the Board of Directors, as the case may be.

“Officers’ Certificate” means, with respect to any Person, a certificate signed by the Chairman, Chief Executive Officer, President or any Senior or Executive Vice President and the Chief Financial Officer or any Treasurer of such Person, that shall comply with applicable provisions of this Indenture.

“Opinion of Counsel” means a written opinion from legal counsel, which counsel is reasonably acceptable to the Trustee. The counsel may be an employee of or counsel to the Company.

“Person” means any individual, corporation, limited liability company, partnership, joint venture, association, joint-stock company, trust, unincorporated organization or government (including any agency or political subdivision thereof).

“Redemption Date,” when used with respect to any Security to be redeemed, means the date fixed for such redemption pursuant to this Indenture.

“Responsible Officer,” when used with respect to the Trustee, means any officer within the corporate trust department or division of the Trustee (or any successor group of the Trustee) or any other officer of the Trustee customarily performing functions similar to those performed by any of the above designated officers, and also means, with respect to a particular corporate trust matter, any other officer to whom such matter is referred because of his knowledge of and familiarity with the particular subject.

“SEC” means the United States Securities and Exchange Commission as constituted from time to time, or any successor performing substantially the same functions.

“Securities” means the securities that are issued under this Indenture, as amended or supplemented from time to time pursuant to this Indenture.

“Securities Act” means the Securities Act of 1933, as amended.

“Series” or “Series of Securities” means each series of debentures, notes or other debt instruments of the Company created pursuant to Sections 2.1 and 2.2.

“Significant Subsidiary” means (i) any direct or indirect Subsidiary of the Company that would be a “significant subsidiary” as defined in Article 1, Rule 1-02 of Regulation S-X, promulgated pursuant to the Securities Act, as such regulation is in effect on the date hereof, or (ii) any group of direct or indirect Subsidiaries of the Company that, taken together as a group, would be a “significant subsidiary” as defined in Article 1, Rule 1-02 of Regulation S-X, promulgated pursuant to the Securities Act, as such regulation is in effect on the date hereof.

“Stated Maturity,” when used with respect to any Security or any installment of principal thereof or interest thereon, means the date specified in such Security as the fixed date on which the principal of such Security, or such installment of principal or interest, is due and payable, and when used with respect to any other Indebtedness, means the date specified in the instrument governing such Indebtedness as the fixed date on which the principal of such Indebtedness, or any installment of interest thereon, is due and payable.

“Subsidiary” of any specified Person means any corporation, limited liability company, partnership, joint venture, association or other business entity, whether now existing or hereafter organized or acquired, (i) in the case of a corporation, of which more than 50% of the total voting power of the Capital Stock entitled (without regard to the occurrence of any contingency) to vote in the election of directors thereof is held, directly or indirectly, by such Person or any of its Subsidiaries; or (ii) in the case of a partnership, joint venture, association or other business entity, with respect to which such Person or any of its Subsidiaries has the power to direct or cause the direction of the management and policies of such entity by contract or otherwise, or if in accordance with GAAP such entity is consolidated with such Person for financial statement purposes.

“TIA” means the Trust Indenture Act of 1939 (15 U.S. Code Section 77aaa-77bbb) as in effect on the date of this Indenture (except as provided in Section 8.3).

“Trustee” means the party named as such in this Indenture until a successor replaces it pursuant to this Indenture, and thereafter means the successor, and if at any time there is more than one such Person, “Trustee” as used with respect to the Securities of any Series shall mean the Trustee with respect to Securities of that Series.

“U.S. Government Obligations” means direct non-callable 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.

1.2. OTHER DEFINITIONS.

The definitions of the following terms may be found in the sections indicated as follows:

TERM	DEFINED IN SECTION
“Bankruptcy Law”	6.1
“Business Day”	10.7
“Covenant Defeasance”	9.3
“Custodian”	6.1
“Event of Default”	6.1

“Journal”	10.15
“Judgment Currency”	10.16
“Legal Defeasance”	9.2
“Legal Holiday”	10.7
“Market Exchange Rate”	10.15
“New York Paying Agent”	2.4
“Paying Agent”	2.4
“Place of Payment”	10.7
“Registrar”	2.4
“Required Currency”	10.16
“Service Agent”	2.4

1.3. INCORPORATION BY REFERENCE OF TRUST INDENTURE ACT.

Whenever this Indenture refers to a provision of the TIA, the portion of such provision required to be incorporated herein in order for this Indenture to be qualified under the TIA is incorporated by reference in and made a part of this Indenture. The following TIA terms used in this Indenture have the following meanings:

“Commission” means the SEC.

“Indenture securities” means the Securities.

“Indenture securityholder” means a Holder or Securityholder.

“Indenture to be qualified” means this Indenture.

“Indenture trustee” or “institutional trustee” means the Trustee.

“Obligor on the indenture securities” means the Company.

All other terms used in this Indenture that are defined by the TIA, defined in the TIA by reference to another statute or defined by SEC rule have the meanings therein assigned to them.

1.4. RULES OF CONSTRUCTION.

Unless the context otherwise requires:

- (1) a term has the meaning assigned to it herein, whether defined expressly or by reference;
- (2) an accounting term not otherwise defined has the meaning assigned to it in accordance with GAAP;
- (3) “or” is not exclusive;
- (4) words in the singular include the plural, and in the plural include the singular;
- (5) words used herein implying any gender shall apply to each gender; and
- (6) the words “herein”, “hereof” and “hereunder” and other words of similar import refer to this Indenture as a whole and not to any particular Article, Section or other subdivision.

**ARTICLE 2 –
THE SECURITIES**

2.1. ISSUABLE IN SERIES.

The aggregate principal amount of Securities that may be authenticated and delivered under this Indenture is \$ _____, _____. The Securities may be issued in one or more Series. All Securities of a Series shall be identical except as may be set forth in a Board Resolution, a supplemental indenture or an Officers' Certificate detailing the adoption of the terms thereof pursuant to the authority granted under a Board Resolution. In the case of Securities of a Series to be issued from time to time, the Board Resolution, Officers' Certificate or supplemental indenture may provide for the method by which specified terms (such as interest rate, Stated Maturity, record date or date from which interest shall accrue) are to be determined. Securities may differ between Series in respect of any matters, PROVIDED, that all Series of Securities shall be equally and ratably entitled to the benefits of the Indenture.

2.2. ESTABLISHMENT OF TERMS OF SERIES OF SECURITIES.

At or prior to the issuance of any Securities within a Series, the following shall be established (as to the Series generally, in the case of Subsection 2.2(1) and either as to such Securities within the Series or as to the Series generally in the case of Subsections 2.2(2) through 2.2(24)) by a Board Resolution, a supplemental indenture or an Officers' Certificate, in each case, pursuant to authority granted under a Board Resolution:

- (1) the title of the Series (which shall distinguish the Securities of that particular Series from the Securities of any other Series);
- (2) any limit upon the aggregate principal amount of the Securities of the Series which may be authenticated and delivered under this Indenture (except for Securities authenticated and delivered upon registration of transfer of, or in exchange for, or in lieu of, other Securities of the Series pursuant to Section 2.7, 2.8, 2.11, 3.6 or 8.5);
- (3) the price or prices (expressed as a percentage of the principal amount thereof) at which the Securities of the Series will be issued;
- (4) the date or dates on which the principal of the Securities of the Series is payable;
- (5) the rate or rates (which may be fixed or variable) per annum or, if applicable, the method used to determine such rate or rates (including, but not limited to, any commodity, commodity index, stock exchange index or financial index) at which the Securities of the Series shall bear interest, if any, the date or dates from which such interest, if any, shall accrue, the date or dates on which such interest, if any, shall commence and be payable and any regular record date for the interest payable on any Interest Payment Date;
- (6) the place or places where the principal of, and interest and premium, if any, on, the Securities of the Series shall be payable, or the method of such payment, if by wire transfer, mail or other means;
- (7) if applicable, the period or periods within which, the price or prices at which and the terms and conditions upon which the Securities of the Series may be redeemed, in whole or in part, at the option of the Company;
- (8) the obligation, if any, of the Company to redeem or purchase the Securities of the Series pursuant to any sinking fund or analogous provisions or at the option of a Holder thereof, and the period or periods within which, the price or prices at which and the terms and conditions upon which Securities of the Series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;
- (9) the dates, if any, on which and the price or prices at which the Securities of the Series will be repurchased by the Company at the option of the Holders thereof, and other detailed terms and provisions of such repurchase obligations;
- (10) if other than denominations of \$1,000 and any integral multiple thereof, the denominations in which the Securities of the Series shall be issuable;
- (11) the forms of the Securities of the Series in bearer (if to be issued outside of the United States of America) or fully registered form (and, if in fully registered form, whether the Securities will be issuable as Global Securities);
- (12) if other than the principal amount thereof, the portion of the principal amount of the Securities of the Series that shall be payable upon declaration of acceleration of the Maturity thereof pursuant to Section 6.2;

(13) the currency of denomination of the Securities of the Series, which may be Dollars or any Foreign Currency, including, but not limited to, the Euro, and, if such currency of denomination is a composite currency other than the Euro, the agency or organization, if any, responsible for overseeing such composite currency;

(14) the designation of the currency, currencies or currency units in which payment of the principal of, and interest and premium, if any, on, the Securities of the Series will be made;

(15) if payments of principal of, or interest or premium, if any, on, the Securities of the Series are to be made in one or more currencies or currency units other than that or those in which such Securities are denominated, the manner in which the exchange rate with respect to such payments will be determined;

(16) the manner in which the amounts of payment of principal of, or interest and premium, if any, on, the Securities of the Series will be determined, if such amounts 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;

(17) the provisions, if any, relating to any collateral provided for the Securities of the Series;

(18) any addition to or change in the covenants set forth in Articles 4 or 5 that applies to Securities of the Series;

(19) any addition to or change in the Events of Default which applies to any Securities of the Series, any provision for the payment of additional interest or liquidated damages in connection with any Event of Default, and any change in the right of the Trustee or the requisite Holders of such Securities to declare the principal amount thereof due and payable pursuant to Section 6.2;

(20) the terms and conditions, if any, for conversion of the Securities into or exchange of the Securities for shares of common stock, preferred stock, other debt securities or warrants for common stock, preferred stock or other securities of any kind of the Company that apply to Securities of the Series;

(21) any Trustees, depositories, interest rate calculation agents, exchange rate calculation agents or other agents with respect to Securities of such Series if other than those appointed herein;

(22) the terms and conditions, if any, upon which the Securities shall be subordinated in right of payment to other Indebtedness of the Company;

(23) if applicable, that the Securities of the Series, in whole or any specified part, shall be defeasible pursuant to Article 9; and

(24) any other terms of the Securities of the Series (which terms shall not be inconsistent with the provisions of this Indenture, except as permitted by Section 8.1, but which may modify or delete any provision of this Indenture insofar as it applies to such Series).

All Securities of any one Series need not be issued at the same time, and may be issued from time to time, consistent with the terms of this Indenture, if so provided by or pursuant to the Board Resolution, supplemental indenture or Officers' Certificate referred to above, however, the authorized principal amount of any Series may not be increased to provide for issuances of additional Securities of such Series, unless otherwise provided in such Board Resolution, supplemental indenture or Officers' Certificate.

2.3. EXECUTION AND AUTHENTICATION.

The Securities shall be executed on behalf of the Company by two Officers of the Company or an Officer and an Assistant Secretary of the Company. Each such signature may be either manual or facsimile. The Company's seal may be impressed, affixed, imprinted or reproduced on the Securities and may be in facsimile form.

If an Officer whose signature is on a Security no longer holds that office at the time the Security is authenticated, the Security shall nevertheless be valid.

A Security shall not be valid until authenticated by the manual signature of the Trustee or an authenticating agent. The signature shall be conclusive evidence that the Security has been authenticated under this Indenture. The Trustee shall at any time, and from time to time, authenticate Securities for original issue in the principal amount provided in the Board Resolution, supplemental indenture hereto or Officers' Certificate, upon receipt by the Trustee of a Company Order. Such Company Order may authorize authentication and delivery pursuant to oral or electronic instructions from the Company or its duly authorized agent or agents, which oral instructions shall be promptly confirmed in writing. Each Security shall be dated the date of its authentication.

The aggregate principal amount of Securities of any Series outstanding at any time may not exceed any limit upon the maximum principal amount for such Series set forth in the Board Resolution, supplemental indenture hereto or Officers' Certificate delivered pursuant to Section 2.2, except as provided in Section 2.8.

Prior to the issuance of Securities of any Series, the Trustee shall have received and (subject to Section 7.1) shall be fully protected in relying on: (a) the Board Resolution, supplemental indenture hereto or Officers' Certificate establishing the form of the Securities of that Series or of Securities within that Series and the terms of the Securities of that Series or of Securities within that Series, (b) an Officers' Certificate complying with Section 10.4, and (c) an Opinion of Counsel complying with Section 10.4.

The Trustee shall have the right to decline to authenticate and deliver any Securities of any Series: (a) if the Trustee, being advised in writing by outside counsel, determines that such action may not lawfully be taken; or (b) if the Trustee in good faith by its board of directors or trustees, executive committee or a trust committee of directors and/or vice-presidents shall reasonably determine that such action would expose the Trustee to personal liability, or cause it to have a conflict of interest with respect to Holders of any then outstanding Series of Securities.

The Trustee may appoint an authenticating agent acceptable to the Company to authenticate Securities. An authenticating agent may authenticate Securities whenever the Trustee may do so. Any appointment shall be evidenced by an instrument signed by an authorized officer of the Trustee, a copy of which shall be furnished to the Company. Each reference in this Indenture to authentication by the Trustee includes authentication by such agent. An authenticating agent has the same rights as an Agent to deal with the Company or an Affiliate of the Company.

2.4. REGISTRAR AND PAYING AGENT.

The Company shall maintain in each Place of Payment for any Series of Securities (i) an office or agency where such Securities may be presented for registration of transfer or for exchange ("Registrar"), (ii) an office or agency where such Securities may be presented for payment ("Paying Agent") (PROVIDED that the Company shall at all times maintain a Paying Agent in the Borough of Manhattan, City of New York, State of New York (the "New York Paying Agent"), and PROVIDED, FURTHER, that at the option of the Company payment of interest may be made by check mailed to the address of the Person entitled thereto as such address shall appear in the register for the Securities maintained by the Registrar), and (iii) an office or agency where notices and demands to or upon the Company in respect of the Securities and this Indenture may be served ("Service Agent"). The Registrar shall keep a register of the Securities and of their transfer and exchange. The Company may have one or more co-registrars and one or more additional paying agents. The Company shall give prompt written notice to the Trustee of the location, and any change in the location, of such office or agency. If at any time the Company shall fail to maintain any such required office, or to furnish the Trustee with the address thereof, such presentations, surrenders, notices and demands may be made or served at the address of the Trustee as set forth in Section 10.2. If the Company acts as Paying Agent, it shall segregate the money held by it for the payment of principal of, and interest and premium, if any, on, the Securities and hold it as a separate trust fund. The Company may change any Paying Agent, Registrar, co-registrar or any other Agent without notice to any Securityholder.

The Company may also from time to time designate one or more other offices or agencies where the Securities may be presented or surrendered for any or all such purposes, and may from time to time rescind such designations; PROVIDED, HOWEVER, that no such designation or rescission shall in any manner relieve the Company of its obligation to maintain an office or agency in each Place of Payment for Securities of any Series for such purposes. The Company hereby initially designates the Corporate Trust Office of the Trustee as such office of the Company. The Company shall give prompt written notice to the Trustee of such designation or rescission, and of any change in the location of any such other office or agency.

The Company shall enter into an appropriate agency agreement with any Registrar or Paying Agent not a party to this Indenture. The agreement shall implement the provisions of this Indenture that relate to such Agent. The Company shall notify the Trustee of the name and address of any such Agent. If the Company fails to maintain a Registrar or Paying Agent, or agent for service of notices and demands, or fails to give the foregoing notice, the Trustee shall act as such. The Company hereby appoints the Trustee as the initial Registrar, Paying Agent and Service Agent for each Series unless another Registrar, Paying Agent or Service Agent, as the case may be, is appointed prior to the time Securities of that Series are first issued. The Company designates, as the New York Paying Agent, with offices at .

2.5. PAYING AGENT TO HOLD ASSETS IN TRUST.

The Trustee as Paying Agent shall, and the Company shall require each Paying Agent other than the Trustee to agree in writing that each Paying Agent shall, hold in trust for the benefit of the Holders of any Series of Securities or the Trustee all assets held by the Paying Agent for the payment of principal of, or interest or premium, if any, on, such Series of Securities (whether such assets have been distributed to it by the Company or any other obligor on such Series of Securities), and the Company and the Paying Agent shall notify the Trustee in writing of any Default by the Company (or any other obligor on such Series of Securities) in making any such payment. The Company at any time may require a Paying Agent to distribute all assets held by it to the Trustee and account for any assets disbursed, and the Trustee may, at any time during the continuance of any payment default with respect to any Series of

Securities, upon written request to a Paying Agent, require such Paying Agent to distribute all assets held by it to the Trustee and to account for any assets distributed. Upon distribution to the Trustee of all assets that shall have been delivered by the Company to the Paying Agent, the Paying Agent shall have no further liability for such assets.

2.6. SECURITYHOLDER LISTS.

The Trustee shall preserve in as current a form as is reasonably practicable the most recent list available to it of the names and addresses of Securityholders of each Series of Securities. If the Trustee is not the Registrar, the Company shall furnish to the Trustee as of each regular record date for the payment of interest on the Securities of a Series and before each related Interest Payment Date, and at such other times as the Trustee may request in writing, a list in such form and as of such date as the Trustee may reasonably require of the names and addresses of Securityholders of each Series of Securities.

2.7. TRANSFER AND EXCHANGE.

When Securities of a Series are presented to the Registrar with a request to register the transfer thereof, the Registrar shall register the transfer as requested if the requirements of applicable law are met, and when such Securities of a Series are presented to the Registrar with a request to exchange them for an equal principal amount of other authorized denominations of Securities of the same Series, the Registrar shall make the exchange as requested. To permit transfers and exchanges, upon surrender of any Security for registration of transfer at the office or agency maintained pursuant to Section 2.4, the Company shall execute and the Trustee shall authenticate Securities at the Registrar's request.

If Securities are issued as Global Securities, the provisions of Section 2.15 shall apply.

All Securities issued upon any registration of transfer or exchange of Securities shall be the valid obligations of the Company, evidencing the same debt, and entitled to the same benefits under this Indenture, as the Securities surrendered upon such registration of transfer or exchange.

Every Security presented or surrendered for registration of transfer or for exchange shall (if so required by the Company or the Registrar or a co-registrar) be duly endorsed, or be accompanied by a written instrument of transfer in form satisfactory to the Company and the Registrar or a co-registrar, duly executed by the Holder thereof or his attorney duly authorized in writing.

Any exchange or transfer shall be without charge, except that the Company may require payment by the Holder of a sum sufficient to cover any tax or other governmental charge that may be imposed in relation to a transfer or exchange, but this provision shall not apply to any exchange pursuant to Section 2.11, 3.6 or 8.5. The Trustee shall not be required to register transfers of Securities of any Series, or to exchange Securities of any Series, for a period of 15 days before the record date for selection for redemption of such Securities. The Trustee shall not be required to exchange or register transfers of Securities of any Series called or being called for redemption in whole or in part, except the unredeemed portion of such Security being redeemed in part.

2.8. REPLACEMENT SECURITIES.

If a mutilated Security is surrendered to the Trustee, or if the Holder of a Security presents evidence to the satisfaction of the Company and the Trustee that the Security has been lost, destroyed or wrongfully taken, the Company shall issue and the Trustee shall authenticate a replacement Security of the same Series and of like tenor and principal amount and bearing a number not contemporaneously outstanding. An indemnity bond may be required by the Company or the Trustee that is sufficient in the reasonable judgment of the Company or the Trustee, as the case may be, to protect the Company, the Trustee or any Agent from any loss which any of them may suffer if a Security is replaced. The Company may charge such Holder for the Company's out-of-pocket expenses in replacing a Security, including the fees and expenses of the Trustee. Every replacement Security shall constitute an original additional obligation of the Company, whether or not the destroyed, lost or stolen Security shall be at any time enforceable by anyone, and shall be entitled to all the benefits of this Indenture equally and proportionately with any and all other Securities of that Series duly issued hereunder.

2.9. OUTSTANDING SECURITIES.

Securities outstanding at any time are all Securities authenticated by the Trustee, except for those canceled by it, those delivered to it for cancellation and those described in this Section 2.9 as not outstanding.

If a Security is replaced pursuant to Section 2.8 (other than a mutilated Security surrendered for replacement), it ceases to be outstanding until the Company and the Trustee receive proof satisfactory to each of them that the replaced Security is held by a bona fide purchaser. A mutilated Security ceases to be outstanding upon surrender of such Security and replacement thereof pursuant to Section 2.8.

If a Paying Agent holds on a Redemption Date or the Stated Maturity money sufficient to pay the principal of, premium, if any, and accrued interest on, Securities payable on that date, and is not prohibited from paying such money to the Holders thereof pursuant to the terms of this Indenture (PROVIDED, that if such Securities are to be redeemed, notice of such redemption has been duly given pursuant to this Indenture or provision therefor satisfactory to the Trustee has been made), then on and after that date such Securities cease to be outstanding and interest on them ceases to accrue.

A Security does not cease to be outstanding solely because the Company or an Affiliate holds the Security.

2.10. WHEN TREASURY SECURITIES DISREGARDED; DETERMINATION OF HOLDERS' ACTION.

In determining whether the Holders of the required aggregate principal amount of the Securities of any Series have concurred in any direction, waiver or consent, the Securities of any Series owned by the Company or any other obligor on such Securities, or by any Affiliate of any of them, shall be disregarded, except that for the purposes of determining whether the Trustee shall be protected in relying on any such direction, waiver or consent, only Securities of such Series which the Trustee actually knows are so owned shall be so disregarded. Securities of such Series so owned which have been pledged in good faith shall not be disregarded if the pledgee establishes to the satisfaction of the Trustee the pledgee's right so to act with respect to the Securities of such Series and that the pledgee is not the Company or any other obligor on the Securities of such Series, or an Affiliate of any of them.

2.11. TEMPORARY SECURITIES.

Until definitive Securities are ready for delivery, the Company may prepare and execute, and the Trustee shall authenticate, temporary Securities. Temporary Securities shall be substantially in the form, and shall carry all rights, of definitive Securities, but may have variations that the Company considers appropriate for temporary Securities. Without unreasonable delay, the Company shall prepare and execute, and the Trustee shall authenticate, definitive Securities in exchange for temporary Securities without charge to the Holder.

2.12. CANCELLATION.

All Securities surrendered for payment, redemption or registration of transfer or exchange, or for credit against any sinking fund payment, shall, if surrendered to any Person other than the Trustee, be delivered to the Trustee for cancellation. The Company may at any time deliver to the Trustee for cancellation any Securities previously authenticated and delivered hereunder which the Company may have acquired in any manner whatsoever, and may deliver to the Trustee (or to any other Person for delivery to the Trustee) for cancellation any Securities previously authenticated hereunder which the Company has not issued and sold. The Registrar and the Paying Agent shall forward to the Trustee any Securities surrendered to them for transfer, exchange or payment. The Trustee or, at the direction of the Trustee, the Registrar or the Paying Agent, and no one else, shall cancel, and at the written request of the Company shall dispose of, all Securities surrendered for transfer, exchange, payment or cancellation. If the Company shall acquire any of the Securities, such acquisition shall not operate as a redemption or satisfaction of the Indebtedness represented by such Securities unless and until the same are surrendered to the Trustee for cancellation pursuant to this Section 2.12. No Securities shall be authenticated in lieu of or in exchange for any Securities cancelled as provided in this Section 2.12, except as expressly permitted by this Indenture.

2.13. PAYMENT OF INTEREST; DEFAULTED INTEREST; COMPUTATION OF INTEREST.

Except as otherwise provided as contemplated by Section 2.2 with respect to any Series of Securities, interest on any Security which is payable, and is punctually paid or duly provided for, on any Interest Payment Date shall be paid to the Person in whose name that Security is registered at the close of business on the regular record date for such interest, as provided in the Board Resolution, supplemental indenture hereto or Officers' Certificate establishing the terms of such Series.

If the Company defaults in a payment of interest on the Securities, it shall pay the defaulted amounts, plus any interest payable on defaulted amounts pursuant to Section 4.1, to the Persons who are Securityholders on a subsequent special record date, which date shall be the 15th day next preceding the date fixed by the Company for the payment of defaulted interest, or the next succeeding Business Day if such date is not a Business Day. At least 15 days before the special record date, the Company shall mail or cause to be mailed to each Securityholder, with a copy to the Trustee, a notice that states the special record date, the payment date and the amount of defaulted interest, and interest payable on such defaulted interest, if any, to be paid.

Except as otherwise specified as contemplated by Section 2.2 for Securities of any Series, interest on the Securities of each Series shall be computed on the basis of a 360-day year of twelve 30-day months.

2.14. CUSIP NUMBER.

The Company in issuing the Securities may use one or more "CUSIP" numbers, and, if the Company does so, the Trustee shall use the CUSIP number(s) in notices of redemption or exchange as a convenience to Holders, PROVIDED, that any such notice may state that no representation is made as to the correctness or accuracy of the CUSIP number(s) printed in the notice or on the Securities,

and that reliance may be placed only on the other identification numbers printed on the Securities, and that any such redemption or exchange shall not be affected by any defect in or omission of any such numbers.

2.15. PROVISIONS FOR GLOBAL SECURITIES.

(a) A Board Resolution, a supplemental indenture hereto or an Officers' Certificate shall establish whether the Securities of a Series shall be issued in whole or in part in the form of one or more Global Securities, and the Depository for such Global Securities or Securities.

(b) Notwithstanding any provisions to the contrary contained in Section 2.7 and in addition thereto, if, and only if the Depository (i) at any time is unwilling or unable to continue as Depository for such Global Security or ceases to be a clearing agency registered under the Exchange Act and (ii) a successor Depository is not appointed by the Company within 90 days after the date the Company is so informed in writing or becomes aware of the same, the Company promptly will execute and deliver to the Trustee definitive Securities, and the Trustee, upon receipt of a Company Request for the authentication and delivery of such definitive Securities (which the Company will promptly execute and deliver to the Trustee) and an Officers' Certificate to the effect that such Global Security shall be so exchangeable, will authenticate and deliver definitive Securities, without charge, registered in such names and in such authorized denominations as the Depository shall direct in writing (pursuant to instructions from its direct and indirect participants or otherwise) in an aggregate principal amount equal to the principal amount of the Global Security with like tenor and terms. Upon the exchange of a Global Security for definitive Securities, such Global Security shall be canceled by the Trustee. Unless and until it is exchanged in whole or in part for definitive Securities, as provided in this Section 2.15(b), a Global Security may not be transferred except as a whole by the Depository with respect to such Global Security to a nominee of such Depository, by a nominee of such Depository to such Depository or another nominee of such Depository or by the Depository or any such nominee to a successor Depository or a nominee of such a successor Depository.

(c) Any Global Security issued hereunder shall bear a legend in substantially the following form:

"This Security is a Global Security within the meaning of the Indenture hereinafter referred to, and is registered in the name of the Depository or a nominee of the Depository. This Security is exchangeable for Securities registered in the name of a Person other than the Depository or its nominee only in the limited circumstances described in the Indenture, and may not be transferred except as a whole by the Depository to a nominee of the Depository, by a nominee of the Depository to the Depository or another nominee of the Depository or by the Depository or any such nominee to a successor Depository or a nominee of such a successor Depository."

(d) The Depository, as a Holder, may appoint agents and otherwise authorize participants to give or take any request, demand, authorization, direction, notice, consent, waiver or other action which a Holder is entitled to give or take under the Indenture.

(e) Notwithstanding the other provisions of this Indenture, unless otherwise specified as contemplated by Section 2.2, payment of the principal of, and interest and premium, if any, on, any Global Security shall be made to the Depository or its nominee in its capacity as the Holder thereof.

(f) Except as provided in Section 2.15(e) above, the Company, the Trustee and any Agent shall treat a Person as the Holder of such principal amount of outstanding Securities of any Series represented by a Global Security as shall be specified in a written statement of the Depository (which may be in the form of a participants' list for such Series) with respect to such Global Security, for purposes of obtaining any consents, declarations, waivers or directions required to be given by the Holders pursuant to this Indenture, PROVIDED, that until the Trustee is so provided with a written statement, it may treat the Depository or any other Person in whose name a Global Security is registered as the owner of such Global Security for the purpose of receiving payment of the principal of, and any premium and (subject to Section 2.13) any interest on, such Global Security and for all other purposes whatsoever, and none of the Company, the Trustee or any agent of the Company or the Trustee shall be affected by notice to the contrary.

2.16. PERSONS DEEMED OWNERS.

Prior to due presentment of a Security for registration of transfer, the Company, the Trustee, the Registrar and any agent of the Company, the Registrar or the Trustee may treat the Person in whose name such Security is registered as the owner of such Security for the purpose of receiving payment of the principal of, and any premium and (subject to Section 2.13) any interest on, such Security and for all other purposes whatsoever, and none of the Company, the Trustee, the Registrar or any agent of the Company, the Trustee or the Registrar shall be affected by notice to the contrary.

**ARTICLE 3 –
REDEMPTION**

3.1. NOTICES TO TRUSTEE.

The Company may, with respect to any Series of Securities, reserve the right to redeem and pay the Series of Securities, or may covenant to redeem and pay the Series of Securities or any part thereof, prior to the Stated Maturity thereof at such time and on such terms as provided for in such Securities or the related Board Resolution, supplemental indenture or Officers' Certificate. If a Series of Securities is redeemable and the Company elects to redeem all or part of such Series of Securities, it shall notify the Trustee of the Redemption Date and the principal amount of Securities to be redeemed at least 45 days (unless a shorter notice shall be satisfactory to the Trustee) before the Redemption Date. Any such notice may be canceled at any time prior to notice of such redemption being mailed to any Holder, and shall thereby be void and of no effect.

3.2. SELECTION BY TRUSTEE OF SECURITIES TO BE REDEEMED.

Unless otherwise indicated for a particular Series of Securities by a Board Resolution, a supplemental indenture or an Officers' Certificate, if fewer than all of the Securities of a Series are to be redeemed, the Trustee shall select the Securities of a Series to be redeemed pro rata, by lot or by any other method that the Trustee considers fair and appropriate (unless the Company specifically directs the Trustee otherwise) and, if such Securities are listed on any securities exchange, by a method that complies with the requirements of such exchange.

The Trustee shall make the selection from Securities of a Series outstanding and not previously called for redemption, and shall promptly notify the Company in writing of the Securities selected for redemption and, in the case of any Security selected for partial redemption, the principal amount thereof to be redeemed at least 35 but not more than 60 days before the Redemption Date. Securities of a Series in denominations of \$1,000 may be redeemed only in whole. The Trustee may select for redemption portions of the principal of Securities of a Series that have denominations larger than \$1,000. Securities of a Series and portions of them it selects shall be in amounts of \$1,000 or, with respect to Securities of any Series issuable in other denominations pursuant to Section 2.2(10), the minimum principal denomination for each Series and integral multiples thereof. Provisions of this Indenture that apply to Securities called for redemption also apply to portions of Securities called for redemption.

3.3. NOTICE OF REDEMPTION.

Unless otherwise indicated for a particular Series by Board Resolution, a supplemental indenture hereto or an Officers' Certificate, at least 30 days, and no more than 60 days, before a Redemption Date, the Company shall mail, or cause to be mailed, a notice of redemption by first-class mail to each Holder of Securities to be redeemed at his or her last address as the same appears on the registry books maintained by the Registrar. The notice shall identify the Securities to be redeemed and shall state:

- (1) the Redemption Date;
- (2) the redemption price, and that such redemption price shall become due and payable on the Redemption Date;
- (3) if any Security of a Series is being redeemed in part, the portion of the principal amount of such Security of a Series to be redeemed and that, after the Redemption Date and upon surrender of such Security of a Series, a new Security or Securities in principal amount equal to the unredeemed portion will be issued;
- (4) the name and address of the Paying Agent;
- (5) that Securities of a Series called for redemption must be surrendered to the Paying Agent to collect the redemption price, and the place or places where each such Security is to be surrendered for such payment;
- (6) that, unless the Company defaults in making the redemption payment, interest on the Securities of a Series called for redemption ceases to accrue on the Redemption Date, and the only remaining right of the Holders of such Securities is to receive payment of the redemption price upon surrender to the Paying Agent of the Securities redeemed;
- (7) if fewer than all of the Securities of a Series are to be redeemed, the identification of the particular Securities of a Series (or portion thereof) to be redeemed, as well as the aggregate principal amount of Securities of a Series to be redeemed and the aggregate principal amount of Securities of a Series to be outstanding after such partial redemption.
- (8) the CUSIP number, if any, printed on the Securities being redeemed; and
- (9) that no representation is made as to the correctness or accuracy of the CUSIP number, if any, listed in such notice or printed on the Securities.

At the Company's request, the Trustee shall give the notice of redemption in the Company's name and at the Company's sole expense.

3.4. EFFECT OF NOTICE OF REDEMPTION.

Once the notice of redemption described in Section 3.3 is mailed, Securities of a Series called for redemption become due and payable on the Redemption Date and at the redemption price, plus interest, if any, accrued to the Redemption Date. Upon surrender to the Trustee or Paying Agent, such Securities of a Series shall be paid at the redemption price, plus accrued interest, if any, to the Redemption Date; PROVIDED, that if the Redemption Date is after a regular interest payment record date and on or prior to the next Interest Payment Date, the accrued interest shall be payable to the Holder of the redeemed Securities registered on the relevant record date, as specified by the Company in the notice to the Trustee pursuant to Section 3.1.

3.5. DEPOSIT OF REDEMPTION PRICE.

On or prior to the Redemption Date (but no later than 11:00 A.M. Eastern Time on such date), the Company shall deposit with the Paying Agent money sufficient to pay the redemption price of and accrued interest, if any, on all Securities to be redeemed on that date other than Securities or portions thereof called for redemption on that date which have been delivered by the Company to the Trustee for cancellation.

On and after any Redemption Date, if money sufficient to pay the redemption price of, and accrued interest on, Securities called for redemption shall have been made available in accordance with the preceding paragraph and the Company and the Paying Agent are not prohibited from paying such moneys to Holders, the Securities called for redemption will cease to accrue interest and the only right of the Holders of such Securities will be to receive payment of the redemption price of and, subject to the proviso in Section 3.4, accrued and unpaid interest on such Securities to the Redemption Date. If any Security called for redemption shall not be so paid, interest will be paid, from the Redemption Date until such redemption payment is made, on the unpaid principal of the Security and any interest or premium, if any, not paid on such unpaid principal, in each case, at the rate and in the manner provided in the Securities.

3.6. SECURITIES REDEEMED IN PART.

Upon surrender of a Security of a Series that is redeemed in part, the Company shall execute, and the Trustee shall authenticate, for a Holder a new Security of the same Series equal in principal amount to the unredeemed portion of the Security surrendered.

ARTICLE 4 – COVENANTS

4.1. PAYMENT OF SECURITIES.

The Company shall pay the principal of, and interest and premium, if any, on, each Series of Securities on the dates and in the manner provided in such Securities and this Indenture.

An installment of principal or interest shall be considered paid on the date it is due if the Trustee or Paying Agent holds on that date money designated for and sufficient to pay such installment and is not prohibited from paying such money to the Holders pursuant to the terms of this Indenture or otherwise.

The Company shall pay interest on overdue principal, and overdue interest, to the extent lawful, at the rate specified in the Series of Securities.

4.2. SEC REPORTS.

The Company will deliver to the Trustee within 15 days after the filing of the same with the SEC, copies of the quarterly and annual reports and of the information, documents and other reports, if any, which the Company is required to file with the SEC pursuant to Section 13 or 15(d) of the Exchange Act; PROVIDED, HOWEVER, that each such report or document will be deemed to be so delivered to the Trustee if the Company files such report or document with the SEC through the SEC's EDGAR database no later than the time such report or document is required to be filed with the SEC pursuant to the Exchange Act. Notwithstanding that the Company may not be subject to the reporting requirements of Section 13 or 15(d) of the Exchange Act, the Company will file with the SEC, to the extent permitted, and provide the Trustee with, such quarterly and annual reports and such information, documents and other reports specified in Sections 13 and 15(d) of the Exchange Act. The Company will also comply with the other provisions of TIA Section 314(a).

4.3. WAIVER OF STAY, EXTENSION OR USURY LAWS.

The Company covenants (to the extent that it may lawfully do so) that it will not at any time insist upon, or plead (as a defense or otherwise) or in any manner whatsoever claim or take the benefit or advantage of, any stay, extension, usury or other law which would prohibit or forgive the Company from paying all or any portion of the principal of, and/or interest and premium, if any, on, the Securities as contemplated herein, wherever enacted, now or at any time hereafter in force, or which may affect the covenants or the performance of this Indenture; and the Company hereby expressly waives (to the extent that they may lawfully do so) all benefit or advantage of any such law, and covenants that it will not hinder, delay or impede the execution of any power herein granted to the Trustee, but will suffer and permit the execution of every such power as though no such law had been enacted.

4.4. COMPLIANCE CERTIFICATE.

(a) The Company shall deliver to the Trustee, within 120 days after the end of each fiscal year of the Company, an Officers' Certificate which complies with TIA Section 314(a)(4) stating that a review of the activities of the Company and its Subsidiaries during such fiscal year has been made under the supervision of the signing Officers with a view to determining whether the Company has kept, observed, performed and fulfilled its obligations under this Indenture, and further stating, as to each such Officer signing such certificate, that to the best of his or her knowledge the Company has kept, observed, performed and fulfilled each and every covenant contained in this Indenture and that there is no default in the performance or observance of any of the terms, provisions and conditions hereof (or, if a Default or Event of Default shall have occurred, describing all such Defaults or Events of Default of which he or she may have knowledge and what action the Company is taking or proposes to take with respect thereto) and that to the best of his or her knowledge no event has occurred and remains in existence by reason of which payments on account of the principal of, or interest or premium, if any, on, the Securities is prohibited, or if such event has occurred, a description of the event and what action the Company is taking or proposes to take with respect thereto.

(b)(i) If any Default or Event of Default has occurred and is continuing or (ii) if any Holder seeks to exercise any remedy hereunder with respect to a claimed Default under this Indenture or the Securities, within five Business Days after the Company becoming aware of such occurrence the Company shall deliver to the Trustee an Officers' Certificate specifying such event, notice or other action and what action the Company is taking or proposes to take with respect thereto.

4.5. CORPORATE EXISTENCE.

Subject to Article 5, the Company shall do or cause to be done all things necessary to preserve and keep in full force and effect its corporate existence, in accordance with the organizational documents (as the same may be amended from time to time) of the Company and the rights (charter and statutory), licenses and franchises of the Company; PROVIDED, HOWEVER, that the Company shall not be required to preserve any such right, license or franchise, or its corporate existence, if the Board of Directors shall determine that the preservation thereof is no longer desirable in the conduct of the business of the Company and that the loss thereof is not adverse in any material respect to the Holders.

ARTICLE 5 – SUCCESSOR CORPORATION

5.1. LIMITATION ON CONSOLIDATION, MERGER AND SALE OF ASSETS.

(a) The Company will not, in any transaction or series of transactions, merge or consolidate with or into, or sell, assign, convey, transfer, lease or otherwise dispose of all or substantially all of its properties and assets (as an entirety or substantially as an entirety in one transaction or a series of related transactions), to any Person or Persons, unless at the time of and after giving effect thereto (i) either (A) if the transaction or series of transactions is a merger or consolidation, the Company shall be the surviving Person of such merger or consolidation, or (B) the Person formed by such consolidation or into which the Company is merged or to which the properties and assets of the Company are transferred (any such surviving Person or transferee Person being the "Surviving Entity") shall be a corporation organized and existing under the laws of the United States of America, any state thereof or the District of Columbia, or a corporation or comparable legal entity organized under the laws of a foreign jurisdiction and shall expressly assume by a supplemental indenture executed and delivered to the Trustee, in form reasonably satisfactory to the Trustee, all of the obligations of the Company (including, without limitation, the obligation to pay the principal of, and premium and interest, if any, on, the Securities and the performance of the other covenants) under the Securities of each Series and this Indenture, and in each case, this Indenture shall remain in full force and effect; and (ii) immediately before and immediately after giving effect to such transaction or series of transactions on a pro forma basis (including, without limitation, any Indebtedness incurred or anticipated to be incurred in connection with or in respect of such transaction or series of transactions), no Default or Event of Default shall have occurred and be continuing.

(b) In connection with any consolidation, merger or transfer of assets contemplated by this Section 5.1, the Company shall deliver, or cause to be delivered, to the Trustee, in form and substance reasonably satisfactory to the Trustee, an Officers' Certificate and an Opinion of Counsel, each stating that such consolidation, merger or transfer, and the supplemental indenture in respect thereto,

comply with this Section 5.1, and that all conditions precedent herein provided for relating to such transaction or transactions have been complied with.

5.2. SUCCESSOR PERSON SUBSTITUTED.

Upon any consolidation, merger or transfer of all or substantially all of the assets of the Company in accordance with Section 5.1 above, the successor corporation formed by such consolidation, or into which the Company is merged or to which such transfer is made, shall succeed to, and be substituted for, and may exercise every right and power of, the Company under this Indenture with the same effect as if such successor corporation had been named as the Company herein, and thereafter (except with respect to any such transfer which is a lease) the predecessor corporation shall be relieved of all obligations and covenants under this Indenture and the Securities.

ARTICLE 6 – DEFAULTS AND REMEDIES

6.1. EVENTS OF DEFAULT.

“Events of Default,” wherever used herein with respect to Securities of any Series, means any one of the following events, unless in the establishing Board Resolution, supplemental indenture or Officers’ Certificate, it is provided that such Series shall not have the benefit of said Event of Default:

(1) there is a default in the payment of any principal of, or premium, if any, on, the Securities when the same becomes due and payable at Maturity, upon acceleration, redemption or otherwise;

(2) there is a default in the payment of any interest on any Security of a Series when the same becomes due and payable, and the Default continues for a period of 30 days;

(3) the Company defaults in the observance or performance of any other covenant in the Securities of a Series or in this Indenture for 60 days after written notice from the Trustee or the Holders of not less than 25% in the aggregate principal amount of the Securities of such Series then outstanding, which notice must specify the Default, demand that it be remedied and state that the notice is a “Notice of Default”;

(4) the Company or any Significant Subsidiary pursuant to or within the meaning of any Bankruptcy Law:

(A) commences a voluntary case,

(B) consents to the entry of an order for relief against it in an involuntary case,

(C) consents to the appointment of a Custodian of it or for all or substantially all of its property,

(D) makes a general assignment for the benefit of its creditors, or

(E) generally is not paying its debts as they become due;

(5) a court of competent jurisdiction enters an order or decree under any Bankruptcy Law that:

(A) is for relief against the Company or any Significant Subsidiary in an involuntary case;

(B) appoints a Custodian of the Company or any Significant Subsidiary, or for all or substantially all of the property of the Company or any Significant Subsidiary; or

(C) orders the liquidation of the Company or any Significant Subsidiary, and the order or decree remains unstayed and in effect for 90 consecutive days; or

(6) any other Event of Default provided with respect to Securities of that Series, which is specified in a Board Resolution, a supplemental indenture hereto or an Officers’ Certificate, in accordance with Section 2.2(19).

The term “Bankruptcy Law” means Title 11, U.S. Code, or any similar federal or state law for the relief of debtors. The term “Custodian” means any receiver, trustee, assignee, liquidator or similar official under any Bankruptcy Law.

The Trustee may withhold notice of any Default (except in the payment of the principal of, or interest or premium, if any, on, the Securities) to the Holders of the Securities of any Series in accordance with Section 7.5. When a Default is cured, it ceases to exist.

6.2. ACCELERATION.

If an Event of Default with respect to Securities of any Series at the time outstanding (other than an Event of Default arising under Section 6.1(4) or (5)) occurs and is continuing, the Trustee by written notice to the Company, or the Holders of not less than 25% in aggregate principal amount of the Securities of that Series then outstanding by written notice to the Company and the Trustee, may declare that the entire principal amount of all the Securities of that Series then outstanding plus accrued and unpaid interest to the date of acceleration are immediately due and payable, in which case such amounts shall become immediately due and payable; PROVIDED, HOWEVER, that after such 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 the outstanding Securities of that Series may rescind and annul such acceleration and its consequences if (i) all existing Events of Default, other than the nonpayment of accelerated principal, interest or premium, if any, that has become due solely because of the acceleration, have been cured or waived, (ii) to the extent the payment of such interest is lawful, interest on overdue installments of interest and overdue principal, which has become due otherwise than by such declaration of acceleration, has been paid and (iii) the rescission would not conflict with any judgment or decree. No such rescission shall affect any subsequent Default or impair any right consequent thereto. In case an Event of Default specified in Section 6.1(4) or (5) with respect to the Company occurs, such principal, premium, if any, and interest amount with respect to all of the Securities of that Series shall be due and payable immediately without any declaration or other act on the part of the Trustee or the Holders of the Securities of that Series.

6.3. REMEDIES.

If an Event of Default with respect to Securities of any Series at the time outstanding occurs and is continuing, the Trustee may pursue any available remedy by proceeding at law or in equity to collect the payment of the principal of, or interest and premium, if any, on, the Securities of that Series, or to enforce the performance of any provision of the Securities of that Series or this Indenture.

The Trustee may maintain a proceeding even if it does not possess any of the Securities of that Series or does not produce any of them in the proceeding. A delay or omission by the Trustee or any Securityholder in exercising any right or remedy accruing upon an Event of Default shall not impair the right or remedy or constitute a waiver of or acquiescence in the Event of Default. No remedy is exclusive of any other remedy. All available remedies are cumulative to the extent permitted by law.

6.4. WAIVER OF PAST DEFAULTS AND EVENTS OF DEFAULT.

Subject to Sections 6.2, 6.7 and 8.2, the Holders of a majority in principal amount of the Securities of any Series then outstanding have the right to waive any existing Default or Event of Default with respect to such Series or compliance with any provision of this Indenture (with respect to such Series) or the Securities of such Series. Upon any such waiver, such Default with respect to such Series shall cease to exist, and any Event of Default with respect to such Series arising therefrom shall be deemed to have been cured for every purpose of this Indenture; but no such waiver shall extend to any subsequent or other Default or Event of Default or impair any right consequent thereto. This Section 6.4 shall be in lieu of TIA Section 316(a)(1)(B), and TIA Section 316(a)(1)(B) is hereby expressly excluded from this Indenture and Section as permitted by the TIA.

6.5. CONTROL BY MAJORITY.

Subject to Sections 6.2, 6.7 and 8.2, the Holders of a majority in principal amount of the Securities of any Series then outstanding may direct the time, method and place of conducting any proceeding for any remedy available to the Trustee or exercising any trust or power conferred on the Trustee by this Indenture with respect to such Series. The Trustee, however, may refuse to follow any direction that conflicts with law or this Indenture, or that the Trustee determines may be unduly prejudicial to the rights of another Securityholder, or that may involve the Trustee in personal liability; PROVIDED, that the Trustee may take any other action deemed proper by the Trustee which is not inconsistent with such direction. This Section 6.5 shall be in lieu of TIA Section 316(a)(1)(A), and TIA Section 316(a)(1)(A) is hereby expressly excluded from this Indenture and Section as permitted by the TIA.

6.6. LIMITATION ON SUITS.

Subject to Section 6.7, a Securityholder may not institute any proceeding or pursue any remedy with respect to this Indenture or the Securities of a Series unless:

- (1) the Holder gives to the Trustee written notice of a continuing Event of Default with respect to the Securities of that Series;
- (2) the Holders of at least 25% in aggregate principal amount of the Securities of such Series then outstanding make a written request to the Trustee to pursue the remedy;

(3) such Holder or Holders offer to the Trustee indemnity reasonably satisfactory to the Trustee against any loss, liability or expense to be incurred in compliance with such request;

(4) the Trustee does not comply with the request within 60 days after receipt of the request and the offer of indemnity; and

(5) no direction inconsistent with such written request has been given to the Trustee during such 60-day period by the Holders of a majority in aggregate principal amount of the Securities of such Series then outstanding.

A Securityholder may not use this Indenture to prejudice the rights of another Securityholder, or to obtain a preference or priority over another Securityholder.

6.7. RIGHTS OF HOLDERS TO RECEIVE PAYMENT.

Notwithstanding any other provision of this Indenture, the right of any Holder of a Security of a Series to receive payment of the principal of, and interest and premium, if any, on, the Security of such Series on or after the respective due dates expressed in the Security of such Series, or to bring suit for the enforcement of any such payment on or after such respective dates, is absolute and unconditional, and shall not be impaired or affected without the consent of the Holder.

6.8. COLLECTION SUIT BY TRUSTEE.

If an Event of Default in payment of principal, interest or premium, if any, specified in Section 6.1(1) or (2) with respect to Securities of any Series at the time outstanding occurs and is continuing, the Trustee may recover judgment in its own name and as trustee of an express trust against the Company (or any other obligor on the Securities of that Series) for the whole amount of unpaid principal and premium, if any, and accrued interest remaining unpaid, together with interest on overdue principal and premium, if any, and, to the extent that payment of such interest is lawful, interest on overdue installments of interest, in each case at the rate then borne by the Securities of that Series, and such further amounts as shall be sufficient to cover the costs and expenses of collection, including the reasonable compensation, expenses, disbursements and advances of the Trustee, its agents and counsel, as set forth in Section 7.7.

6.9. TRUSTEE MAY FILE PROOFS OF CLAIM.

The Trustee may file such proofs of claim and other papers or documents, and take other actions (including sitting on a committee of creditors), as may be necessary or advisable in order to have the claims of the Trustee (including any claim for the reasonable compensation, expenses, disbursements and advances of the Trustee, its agents and counsel) and the Securityholders allowed in any judicial proceedings relative to the Company (or any other obligor on the Securities), any of their respective creditors or any of their respective property, and the Trustee shall be entitled and empowered to collect and receive any monies or other property payable or deliverable on any such claims, and to distribute the same after deduction of its charges and expenses to the extent that any such charges and expenses are not paid out of the estate in any such proceedings, and any custodian in any such judicial proceeding is hereby authorized by each Securityholder to make such payments to the Trustee, and in the event that the Trustee shall consent to the making of such payments directly to the Securityholders, to pay to the Trustee any amount due to it for the reasonable compensation, expenses, disbursements and advances of the Trustee, its agents and counsel, and any other amounts due the Trustee under Section 7.7.

Nothing herein contained shall be deemed to authorize the Trustee to authorize or consent to, or accept or adopt on behalf of any Securityholder, any plan of reorganization, arrangement, adjustment or composition affecting the Securities of a Series or the rights of any Holder thereof, or to authorize the Trustee to vote in respect of the claim of any Securityholder in any such proceedings.

6.10. PRIORITIES.

If the Trustee collects any money pursuant to this Article 6, it shall pay out the money in the following order:

FIRST: to the Trustee for amounts due under Section 7.7;

SECOND: to Securityholders for amounts then due and unpaid for the principal of, and interest and premium, if any, on, the Securities in respect of which, or for the benefit of which, such money has been collected, ratably, without preference or priority of any kind, according to the amounts due and payable on such Securities; for principal and any premium and interest, respectively; and

THIRD: to the Company.

The Trustee may fix a record date and payment date for any payment to Securityholders pursuant to this Section 6.10. At least 15 days before such record date, the Trustee shall mail to each Securityholder a notice that states the record date, the payment date and amount to be paid.

6.11. UNDERTAKING FOR COSTS.

In any suit for the enforcement of any right or remedy under this Indenture, or in any suit against the Trustee for any action taken or omitted by it as Trustee, a court in its discretion may require the filing by any party litigant in the suit of an undertaking to pay the costs of the suit, and the court in its discretion may assess reasonable costs, including reasonable attorneys' fees, against any party litigant in the suit, having due regard to the merits and good faith of the claims or defenses made by the party litigant. This Section 6.11 does not apply to a suit by the Trustee, a suit by a Holder pursuant to Section 6.7 or a suit by Holders of more than 10% in principal amount of the Securities of a Series then outstanding.

ARTICLE 7 – TRUSTEE

7.1. DUTIES OF TRUSTEE.

(a) If an Event of Default has occurred and is continuing, the Trustee shall exercise such of the rights and powers vested in it by this Indenture and use the same degree of care and skill in their exercise as a prudent Person would exercise or use under the same circumstances in the conduct of his own affairs.

(b) Except during the continuance of an Event of Default:

(1) The Trustee need perform only those duties that are specifically set forth in this Indenture, and no covenants or obligations shall be implied in this Indenture against the Trustee.

(2) In the absence of bad faith on its part, the Trustee may conclusively rely, as to the truth of the statements and the correctness of the opinions expressed therein, upon certificates or opinions furnished to the Trustee and conforming to the requirements of this Indenture, but, in the case of any such certificates or opinions which by any provision hereof are specifically required to be furnished to the Trustee, the Trustee shall be under a duty to examine the same to determine whether or not they conform to the requirements of this Indenture.

(c) The Trustee may not be relieved from liability for its own negligent action, its own negligent failure to act or its own willful misconduct, except that:

(1) This paragraph does not limit the effect of paragraph (b) of this Section 7.1.

(2) The Trustee shall not be liable for any error of judgment made in good faith by a Responsible Officer, unless it is proved that the Trustee was negligent in ascertaining the pertinent facts.

(3) The Trustee shall not be liable with respect to any action it takes or omits to take in good faith in accordance with a direction received by it pursuant to Sections 6.2 and 6.5.

(d) No provision of this Indenture shall require the Trustee to expend or risk its own funds, or otherwise incur any financial liability, in the performance of any of its rights or powers if it shall have reasonable grounds for believing that repayment of such funds or adequate indemnity satisfactory to it against such risk or liability is not reasonably assured to it.

(e) Whether or not therein expressly so provided, paragraphs (a), (b), (c) and (d) of this Section 7.1 shall govern every provision of this Indenture that in any way relates to the Trustee.

(f) The Trustee and Paying Agent shall not be liable for interest on any money received by either of them, except as the Trustee and Paying Agent may agree in writing with the Company. Money held in trust by the Trustee need not be segregated from other funds except to the extent required by the law.

(g) The Paying Agent, the Registrar and any authenticating agent shall be entitled to the protections, immunities and standard of care set forth in paragraphs (a), (b), (c), (d) and (f) of this Section 7.1 and in Section 7.2 with respect to the Trustee.

7.2. RIGHTS OF TRUSTEE.

(a) Subject to Section 7.1:

(1) The Trustee may rely on, and shall be protected in acting or refraining from acting upon, any document reasonably believed by it to be genuine and to have been signed or presented by the proper Person. The Trustee need not investigate any fact or matter stated in the document.

(2) Before the Trustee acts or refrains from acting, it may require an Officers' Certificate or an Opinion of Counsel, or both, which shall conform to the provisions of Section 10.5. The Trustee shall be protected and shall not be liable for any action it takes or omits to take in good faith in reliance on such certificate or opinion.

(3) The Trustee may act through agents and attorneys, and shall not be responsible for the misconduct or negligence of any agent appointed by it with due care.

(4) The Trustee shall not be liable for any action it takes or omits to take in good faith which it reasonably believes to be authorized or within its rights or powers.

(5) The Trustee may consult with counsel reasonably acceptable to the Trustee, which may be counsel to the Company, and the advice or opinion of such counsel as to matters of law shall be full and complete authorization and protection from liability in respect of any action taken, omitted or suffered by it hereunder in good faith and in accordance with the advice or opinion of such counsel.

(6) The Trustee shall be under no obligation to exercise any of the rights or powers vested in it by this Indenture at the request, order or direction of any of the Holders pursuant to the provisions of this Indenture, unless such Holders shall have offered to the Trustee reasonable security or indemnity against the costs, expenses and liabilities which may be incurred therein or thereby.

(7) The Trustee shall not be deemed to have knowledge of any fact or matter (including, without limitation, a Default or Event of Default) unless such fact or matter is known to a Responsible Officer of the Trustee.

(8) Unless otherwise expressly provided herein or in the Securities of a Series or the related Board Resolution, supplemental indenture or Officers' Certificate, the Trustee shall not have any responsibility with respect to reports, notices, certificates or other documents filed with it hereunder, except to make them available for inspection, at reasonable times, by Securityholders, it being understood that delivery of such reports, information and documents to the Trustee is for informational purposes only and the Trustee's receipt of such shall not constitute constructive notice of any information contained therein or determinable from information contained therein, including the Company's compliance with any of its covenants hereunder (except as set forth in Section 4.4).

7.3. INDIVIDUAL RIGHTS OF TRUSTEE.

The Trustee in its individual or any other capacity may become the owner or pledgee of Securities, and may make loans to, accept deposits from, perform services for or otherwise deal with the Company, or any Affiliate thereof, with the same rights it would have if it were not Trustee. Any Agent may do the same with like rights. The Trustee, however, shall be subject to Sections 7.10 and 7.11.

7.4. TRUSTEE'S DISCLAIMER.

The Trustee makes no representation as to the validity or adequacy of this Indenture or the Securities (except that the Trustee represents that it is duly authorized to execute and deliver this Indenture and authenticate the Securities and perform its obligations hereunder), and the Trustee shall not be accountable for the Company's use of the proceeds from the sale of Securities or any money paid to the Company pursuant to the terms of this Indenture, and the Trustee shall not be responsible for any statement in the Securities other than its certificates of authentication.

7.5. NOTICE OF DEFAULT.

If a Default or an Event of Default occurs and is continuing with respect to the Securities of any Series, and if it is known to the Trustee, the Trustee shall mail to each Securityholder of the Securities of that Series notice of the Default or the Event of Default, as the case may be, within 90 days after it occurs or, if later, after a Responsible Officer of the Trustee has knowledge of such Default or Event of Default (except if such Default or Event of Default has been validly cured or waived before the giving of such notice). Except in the case of a Default or an Event of Default in payment of the principal of, or interest or premium, if any, on, any Security of any Series, the Trustee may withhold the notice if and so long as the Board of Directors of the Trustee, the executive committee or any trust committee of such board and/or its Responsible Officers in good faith determine(s) that withholding the notice is in the interests of the Securityholders of that Series.

7.6. REPORTS BY TRUSTEE TO HOLDERS.

If and to the extent required by the TIA, within 60 days after April 1 of each year, commencing the April 1 following the date of this Indenture, the Trustee shall mail to each Securityholder a brief report dated as of such April 1 that complies with TIA Section 313(a). The Trustee also shall comply with TIA Sections 313(b) and 313(c).

A copy of each report at the time of its mailing to Securityholders shall be filed with the SEC and any stock exchange on which the Securities of that Series are listed. The Company shall promptly notify the Trustee when the Securities of any Series are listed on any stock exchange or any delisting thereof, and the Trustee shall comply with TIA Section 313(d).

7.7. COMPENSATION AND INDEMNITY.

The Company shall pay to the Trustee from time to time reasonable compensation for its services. The Trustee's compensation shall not be limited by any provision of law on compensation of a trustee of an express trust. The Company shall reimburse the Trustee within 45 days after receipt of request for all reasonable out-of-pocket disbursements and expenses incurred or made by it in connection with its duties under this Indenture, including the reasonable compensation, disbursements and expenses of the Trustee's agents and counsel.

The Company shall indemnify the Trustee for, and hold it harmless against, any and all loss or liability incurred by it in connection with the acceptance or performance of its duties under this Indenture including the reasonable costs and expenses of defending itself against any claim or liability in connection with the exercise or performance of any of its powers or duties hereunder. The Trustee shall notify the Company promptly of any claim asserted against the Trustee for which it may seek indemnity.

The failure by the Trustee to so notify the Company shall not however relieve the Company of its obligations. Notwithstanding the foregoing, the Company need not reimburse the Trustee for any expense or indemnify it against any loss or liability incurred by the Trustee through its negligence or bad faith. To secure the payment obligations of the Company in this Section 7.7, the Trustee shall have a lien prior to the Securities of any Series on all money or property held or collected by the Trustee except such money or property held in trust to pay the principal of, interest and premium, if any, on particular Securities of that Series.

When the Trustee incurs expenses or renders services after an Event of Default specified in Section 6.1(4) or (5) occurs, the expenses and the compensation for the services are intended to constitute expenses of administration under any Bankruptcy Law.

For purposes of this Section 7.7, the term "Trustee" shall include any trustee appointed pursuant to this Article 7.

7.8. REPLACEMENT OF TRUSTEE.

The Trustee may resign with respect to the Securities of one or more Series by so notifying the Company in writing at least 90 days in advance of such resignation.

The Holders of a majority in principal amount of the outstanding Securities of any Series may remove the Trustee with respect to that Series by notifying the removed Trustee in writing and may appoint a successor Trustee with respect to that Series with the consent of the Company, which consent shall not be unreasonably withheld. The Company may remove the Trustee with respect to that Series at its election if:

- (1) the Trustee fails to comply with, or ceases to be eligible under, Section 7.10;
- (2) the Trustee is adjudged a bankrupt or an insolvent, or an order for relief is entered with respect to the Trustee, under any Bankruptcy Law;
- (3) a Custodian or other public officer takes charge of the Trustee or its property; or
- (4) the Trustee otherwise becomes incapable of acting.

(5) If the Trustee resigns or is removed, or if a vacancy exists in the office of Trustee, with respect to any Series of Securities for any reason, the Company shall promptly appoint, by Board Resolution, a successor Trustee.

If a successor Trustee with respect to the Securities of one or more Series does not take office within 60 days after the retiring Trustee resigns or is removed, the retiring Trustee, the Company or the Holders of at least 10% in principal amount of the outstanding Securities of the applicable Series may petition any court of competent jurisdiction for the appointment of a successor Trustee.

If the Trustee with respect to the Securities of one or more Series fails to comply with Section 7.10, any Securityholder of the applicable Series may petition any court of competent jurisdiction for the removal of the Trustee and the appointment of a successor Trustee.

A successor Trustee shall deliver a written acceptance of its appointment to the retiring Trustee and to the Company. Immediately following such delivery, (i) the retiring Trustee with respect to one or more Series shall, subject to its rights under Section 7.7, transfer all property held by it as Trustee with respect to such Series to the successor Trustee, (ii) the resignation or removal of the retiring Trustee shall become effective and (iii) the successor Trustee with respect to such Series shall have all the rights, powers and duties of the Trustee under this Indenture. A successor Trustee with respect to the Securities of one or more Series shall mail notice of its succession to each Securityholder of such Series.

7.9. SUCCESSOR TRUSTEE BY CONSOLIDATION, MERGER OR CONVERSION.

If the Trustee, or any Agent, consolidates with, merges or converts into, or transfers all or substantially all of its corporate trust assets to, another corporation, subject to Section 7.10, the successor corporation without any further act shall be the successor Trustee or Agent, as the case may be.

7.10. ELIGIBILITY; DISQUALIFICATION.

This Indenture shall always have a Trustee who satisfies the requirements of TIA Sections 310(a)(1), (2) and (5) in every respect. The Trustee (or in the case of a Trustee that is a Person included in a bank holding company system, the related bank holding company) shall have a combined capital and surplus of at least \$100,000,000 as set forth in its most recent published annual report of condition. The Trustee shall comply with TIA Section 310(b), including the provision in Section 310(b)(1). In addition, if the Trustee is a Person included in a bank holding company system, the Trustee, independently of such bank holding company, shall meet the capital requirements of TIA Section 310(a)(2). If at any time the Trustee shall cease to be eligible in accordance with the provisions of this Section 7.10, it shall resign immediately in the manner and with the effect specified in this Article 7.

7.11. PREFERENTIAL COLLECTION OF CLAIMS AGAINST COMPANY.

The Trustee shall comply with TIA Section 311(a), excluding any creditor relationship listed in TIA Section 311(b). A Trustee who has resigned or been removed shall be subject to TIA Section 311(a) to the extent indicated therein.

7.12. PAYING AGENTS.

The Company shall cause each Paying Agent other than the Trustee to execute and deliver to it and the Trustee an instrument in which such agent shall agree with the Trustee, subject to the provisions of this Section 7.12:

(1) that it will hold all sums held by it as agent for the payment of the principal of, or interest or premium, if any, on, the Securities (whether such sums have been paid to it by the Company or by any obligor on the Securities) in trust for the benefit of Holders of the Securities or the Trustee;

(2) that it will at any time during the continuance of any Event of Default, upon written request from the Trustee, deliver to the Trustee all sums so held in trust by it together with a full accounting thereof; and

(3) that it will give the Trustee written notice within three Business Days after any failure of the Company (or by any obligor on the Securities) in the payment of any installment of the principal of, or interest or premium, if any, on, the Securities when the same shall be due and payable.

ARTICLE 8 – AMENDMENTS, SUPPLEMENTS AND WAIVERS

8.1. WITHOUT CONSENT OF HOLDERS.

The Company, when authorized by a Board Resolution, and the Trustee may amend or supplement this Indenture or the Securities of one or more Series without notice to or consent of any Securityholder:

(1) to comply with Section 5.1;

(2) to provide for certificated Securities in addition to uncertificated Securities;

(3) to comply with any requirements of the SEC under the TIA;

(4) to cure any ambiguity, defect or inconsistency, or to make any other change herein or in the Securities that does not materially and adversely affect the rights of any Securityholder;

(5) to provide for the issuance of, and establish the form and terms and conditions of, Securities of any Series as permitted by this Indenture; or

(6) to evidence and provide for the acceptance of appointment hereunder by a successor Trustee with respect to the Securities of one or more Series, and to add to or change any of the provisions of this Indenture as shall be necessary to provide for or facilitate the administration of the trusts hereunder by more than one Trustee.

The Trustee is hereby authorized to join with the Company in the execution of any supplemental indenture authorized or permitted by the terms of this Indenture, and to make any further appropriate agreements and stipulations which may be therein contained, but the Trustee shall not be obligated to enter into any such supplemental indenture which adversely affects its own rights, duties or immunities under this Indenture.

8.2. WITH CONSENT OF HOLDERS.

(a) The Company, when authorized by a Board Resolution, and the Trustee may amend or supplement this Indenture or the Securities of one or more Series with the written consent of the Holders of not less than a majority in aggregate principal amount of the outstanding Securities of such Series affected by such amendment or supplement without notice to any Securityholder. The Holders of not less than a majority in aggregate principal amount of the outstanding Securities of each such Series affected by such amendment or supplement may waive compliance by the Company in a particular instance with any provision of this Indenture or the Securities of such Series without notice to any Securityholder. Subject to Section 8.4, without the consent of each Securityholder affected, however, an amendment, supplement or waiver may not:

(1) reduce the amount of Securities whose Holders must consent to an amendment, supplement or waiver to this Indenture or the Securities;

(2) reduce the rate of, or change the time for payment of, interest on any Security;

(3) reduce the principal, or change the Stated Maturity, of any Security, or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation;

(4) make any Security payable in money other than that stated in the Security;

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

(6) waive a Default or Event of Default in the payment of the principal of, or interest or premium, if any, on, any Security (except a rescission of acceleration of the Securities of any Series by the Holders of at least a majority in principal amount of the outstanding Securities of such Series and a waiver of the payment default that resulted from such acceleration);

(7) waive a redemption payment with respect to any Security, or change any of the provisions with respect to the redemption of any Securities;

(8) make any changes in Section 6.6 or this Section 8.2, except to increase any percentage of Securities the Holders of which must consent to any matter; or

(9) take any other action otherwise prohibited by this Indenture to be taken without the consent of each Holder affected thereby.

(b) Upon the request of the Company, accompanied by a Board Resolution authorizing the execution of any such supplemental indenture, and upon the receipt by the Trustee of evidence reasonably satisfactory to the Trustee of the consent of the Securityholders as aforesaid and of the documents described in Section 8.6, the Trustee shall join with the Company in the execution of such supplemental indenture, unless such supplemental indenture affects the Trustee's own rights, duties or immunities under this Indenture, in which case the Trustee may in its discretion, but shall not be obligated to, enter into such supplemental indenture.

(c) It shall not be necessary for the consent of the Holders under this section to approve the particular form of any proposed amendment, supplement or waiver, but it shall be sufficient if such consent approves the substance thereof.

After an amendment or supplement under this Section becomes effective, the Company shall mail to Securityholders a notice briefly describing the amendment or supplement. Any failure of the Company to mail any such notice, or any defect therein, shall not, however, in any way impair or affect the validity of any supplemental indenture.

8.3. COMPLIANCE WITH TRUST INDENTURE ACT.

Every amendment to, or supplement of, this Indenture or the Securities shall comply with the TIA as then in effect.

8.4. REVOCATION AND EFFECT OF CONSENTS.

Until an amendment, supplement, waiver or other action becomes effective, a consent to it by a Holder of a Security is a continuing consent conclusive and binding upon such Holder and every subsequent Holder of the same Security or portion thereof, and of any Security issued upon the transfer thereof or in exchange therefor or in place thereof, even if notation of the consent is not made on any such Security. Any such Holder or subsequent Holder, however, may revoke the consent as to his Security or portion of a Security, if the Trustee receives the notice of revocation before the date the amendment, supplement, waiver or other action becomes effective.

The Company may, but shall not be obligated to, fix a record date for the purpose of determining the Holders entitled to consent to any amendment, supplement or waiver, which record date shall be at least 30 days prior to the first solicitation of such consent. If a record date is fixed, then, notwithstanding the preceding paragraph, those Persons who were Holders at such record date (or their duly designated proxies), and only such Persons, shall be entitled to consent to such amendment, supplement or waiver, or to revoke any consent previously given, whether or not such Persons continue to be Holders after such record date.

After an amendment, supplement, waiver or other action becomes effective, it shall bind every Securityholder, unless it makes a change described in any of clauses (1) through (9) of Section 8.2. In that case, the amendment, supplement, waiver or other action shall bind each Holder of a Security who has consented to it and every subsequent Holder of a Security or portion of a Security that evidences the same debt as the consenting Holder's Security; PROVIDED, that any such waiver shall not impair or affect the right of any Holder to receive payment of the principal of, and interest and premium, if any, on, a Security, on or after the respective due dates expressed in such Security, or to bring suit for the enforcement of any such payment on or after such respective dates without the consent of such Holder.

8.5. NOTATION ON OR EXCHANGE OF SECURITIES.

If an amendment, supplement or waiver changes the terms of a Security of any Series, the Trustee may request the Holder of such Security to deliver it to the Trustee. In such case, the Trustee shall place an appropriate notation on such Security about the changed terms and return it to the Holder. Alternatively, the Company, in exchange for such Security, may issue, and the Trustee shall authenticate, a new security that reflects the changed terms. Failure to make the appropriate notation or issue a new Security shall not affect the validity and effect of such amendment, supplement or waiver.

8.6. TRUSTEE TO SIGN AMENDMENTS, ETC.

The Trustee shall sign any amendment, supplement or waiver authorized pursuant to this Article 8 if the amendment, supplement or waiver does not adversely affect the rights, duties, liabilities or immunities of the Trustee. If it does, the Trustee may, but need not, sign it. In signing or refusing to sign such amendment, supplement or waiver the Trustee shall be entitled to receive and, subject to Section 7.1, shall be fully protected in relying upon an Officers' Certificate and an Opinion of Counsel stating that such amendment, supplement or waiver is authorized or permitted by this Indenture. The Company may not sign an amendment or supplement until the Board of Directors of the Company approves it.

ARTICLE 9 – DISCHARGE OF INDENTURE; DEFEASANCE

9.1. DISCHARGE OF INDENTURE.

The Company may terminate its obligations under the Securities of any Series and this Indenture with respect to such Series, except the obligations referred to in the last paragraph of this Section 9.1, if there shall have been canceled by the Trustee, or delivered to the Trustee for cancellation, all Securities of such Series theretofore authenticated and delivered (other than any Securities of such Series that are asserted to have been destroyed, lost or stolen and that shall have been replaced as provided in Section 2.8) and the Company has paid all sums payable by it hereunder or deposited all required sums with the Trustee.

After such delivery the Trustee upon request shall acknowledge in a writing prepared by or on behalf of the Company the discharge of the Company's obligations under the Securities of such Series and this Indenture, except for those surviving obligations specified below.

Notwithstanding the satisfaction and discharge of this Indenture, the obligations of the Company in Sections 7.7, 9.5 and 9.6 shall survive.

9.2. LEGAL DEFEASANCE.

The Company may at its option, by Board Resolution, be discharged from its obligations with respect to the Securities of any Series on the date upon which the conditions set forth in Section 9.4 below are satisfied (hereinafter, "Legal Defeasance"). For this purpose, such Legal Defeasance means that the Company shall be deemed to have paid and discharged the entire indebtedness represented by the Securities of such Series and to have satisfied all its other obligations under such Securities and this Indenture insofar as such Securities are concerned (and the Trustee, at the expense of the Company, shall, subject to Section 9.6, execute proper instruments acknowledging the same, as are delivered to it by the Company), except for the following, which shall survive until otherwise terminated or discharged hereunder: (A) the rights of Holders of outstanding Securities of such Series to receive solely from the trust funds described in Section 9.4 and as more fully set forth in such section, payments in respect of the principal of, and interest and premium, if any, on, the Securities of such Series when such payments are due, (B) the Company's obligations with respect to the Securities of such Series under Sections 2.4, 2.5, 2.6, 2.7, 2.8 and 2.9, (C) the rights, powers, trusts, duties and immunities of the Trustee hereunder (including claims of, or payments to, the Trustee under or pursuant to Section 7.7) and (D) this Article 9. Subject to compliance with this Article 9, the Company may exercise its option under this Section 9.2 with respect to the Securities of any Series notwithstanding the prior exercise of its option under Section 9.3 below with respect to the Securities of such Series.

9.3. COVENANT DEFEASANCE.

At the option of the Company, pursuant to a Board Resolution, the Company shall be released from its obligations with respect to the outstanding Securities of any Series under Sections 4.2 through 4.5, inclusive, and Section 5.1, with respect to the outstanding Securities of such Series, on and after the date the conditions set forth in Section 9.4 are satisfied (hereinafter, "Covenant Defeasance"). For this purpose, such Covenant Defeasance means that the Company may omit to comply with and shall have no liability in respect of any term, condition or limitation set forth in any such specified section or portion thereof, whether directly or indirectly by reason of any reference elsewhere herein to any such specified Section or portion thereof or by reason of any reference in any such specified section or portion thereof to any other provision herein or in any other document, but the remainder of this Indenture and the Securities of any Series shall be unaffected thereby.

9.4. CONDITIONS TO LEGAL DEFEASANCE OR COVENANT DEFEASANCE.

The following shall be the conditions to application of Section 9.2 or Section 9.3 to the outstanding Securities of a Series:

(1) the Company shall irrevocably have deposited or caused to be deposited with the Trustee (or another trustee satisfying the requirements of Section 7.10 who shall agree to comply with the provisions of this Article 9 applicable to it) as funds in trust for the purpose of making the following payments, specifically pledged as security for, and dedicated solely to, the benefit of the Holders of the Securities, (A) money in an amount, or (B) U.S. Government Obligations or Foreign Government Obligations which through the scheduled payment of principal and interest in respect thereof in accordance with their terms will provide, not later than the due date of any payment, money in an amount, or (C) a combination thereof, sufficient, in the opinion of a nationally recognized firm of independent public accountants expressed in a written certification thereof delivered to the Trustee, to pay and discharge, and which shall be applied by the Trustee (or other qualifying trustee) to pay and discharge, the principal of, and accrued interest and premium, if any, on, the outstanding Securities of such Series at the Stated Maturity of such principal, interest or premium, if any, or on dates for payment and redemption of such principal, interest and premium, if any, selected in accordance with the terms of this Indenture and of the Securities of such Series;

(2) no Event of Default or Default with respect to the Securities of such Series shall have occurred and be continuing on the date of such deposit, or shall have occurred and be continuing at any time during the period ending on the 91st day after the date of such deposit or, if longer, ending on the day following the expiration of the longest preference period under any Bankruptcy Law applicable to the Company in respect of such deposit as specified in the Opinion of Counsel identified in paragraph (8) below (it being understood that this condition shall not be deemed satisfied until the expiration of such period);

(3) such Legal Defeasance or Covenant Defeasance shall not cause the Trustee to have a conflicting interest for purposes of the TIA with respect to any securities of the Company;

(4) such Legal Defeasance or Covenant Defeasance shall not result in a breach or violation of, or constitute default under, any other agreement or instrument to which the Company is a party or by which it is bound;

(5) the Company shall have delivered to the Trustee an Opinion of Counsel stating that, as a result of such Legal Defeasance or Covenant Defeasance, neither the trust nor the Trustee will be required to register as an investment company under the Investment Company Act of 1940, as amended;

(6) in the case of an election under Section 9.2, the Company shall have delivered to the Trustee an Opinion of Counsel stating that (i) the Company has received from, or there has been published by, the Internal Revenue Service a ruling to the effect that or (ii) there has been a change in any applicable Federal income tax law with the effect that, and such opinion shall confirm that, the Holders of the outstanding Securities of such Series or Persons in their positions will not recognize income, gain or loss for Federal income tax purposes solely as a result of such Legal Defeasance and will be subject to 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 such Legal Defeasance had not occurred;

(7) in the case of an election under Section 9.3, the Company shall have delivered to the Trustee an Opinion of Counsel to the effect that the Holders of the outstanding Securities of such Series will not recognize income, gain or loss for Federal income tax purposes as a result of such Covenant Defeasance, and will be subject to Federal income tax on the same amounts, in the same manner and at the same times as would have been the case if such Covenant Defeasance had not occurred;

(8) the Company shall have delivered to the Trustee an Officers' Certificate and an Opinion of Counsel, each stating that all conditions precedent provided for in this Article 9 relating to either the Legal Defeasance under Section 9.2 or the Covenant Defeasance under Section 9.3 (as the case may be) have been complied with;

(9) the Company shall have delivered to the Trustee an Officers' Certificate stating that the deposit under clause (1) was not made by the Company with the intent of defeating, hindering, delaying or defrauding any creditors of the Company or others; and

(10) the Company shall have paid, or duly provided for payment under terms mutually satisfactory to the Company and the Trustee, all amounts then due to the Trustee pursuant to Section 7.7.

9.5. DEPOSITED MONEY AND U.S. AND FOREIGN GOVERNMENT OBLIGATIONS TO BE HELD IN TRUST; OTHER MISCELLANEOUS PROVISIONS.

All money, U.S. Government Obligations and Foreign Government Obligations (including the proceeds thereof) deposited with the Trustee pursuant to Section 9.4 in respect of the outstanding Securities shall be held in trust and applied by the Trustee, in accordance with the provisions of such Securities and this Indenture, to the payment, either directly or through any Paying Agent as the Trustee may determine, to the Holders of such Securities, of all sums due and to become due thereon in respect of principal, accrued interest and premium, if any, but such money need not be segregated from other funds except to the extent required by law.

The Company shall pay and indemnify the Trustee against any tax, fee or other charge imposed on or assessed against the U.S. Government Obligations and Foreign Government Obligations deposited pursuant to Section 9.4 or the principal, interest and premium, if any, received in respect thereof other than any such tax, fee or other charge which by law is for the account of the Holders of the outstanding Securities.

Anything in this Article 9 to the contrary notwithstanding, but subject to payment of any of its outstanding fees and expenses, the Trustee shall deliver or pay to the Company from time to time upon Company Request any money, U.S. Government Obligations or Foreign Government Obligations held by the Trustee as provided in Section 9.4 which, in the opinion of a nationally-recognized firm of independent public accountants expressed in a written certification thereof delivered to the Trustee, are in excess of the amount thereof which would then be required to be deposited to effect an equivalent Legal Defeasance or Covenant Defeasance.

9.6. REINSTATEMENT.

If the Trustee or Paying Agent is unable to apply any money, U.S. Government Obligations or Foreign Government Obligations in accordance with Section 9.1, 9.2, 9.3 or 9.4 by reason of any legal proceeding or by reason of any order or judgment of any court or governmental authority enjoining, restraining or otherwise prohibiting such application, the Company's obligations under this Indenture and the Securities shall be revived and reinstated as though no deposit had occurred pursuant to this Article 9 until such time as the Trustee or Paying Agent is permitted to apply all such money, U.S. Government Obligations or Foreign Government Obligations, as the case may be, in accordance with Section 9.1, 9.2, 9.3 or 9.4; PROVIDED, HOWEVER, that if the Company has made any payment of principal of, or accrued interest or premium, if any, on, any Securities because of the reinstatement of its obligations, the Company shall be subrogated to the rights of the Holders of such Securities to receive such payment from the money, U.S. Government Obligations or Foreign Government Obligations held by the Trustee or Paying Agent.

9.7. MONEYS HELD BY PAYING AGENT.

In connection with the satisfaction and discharge of this Indenture, all moneys then held by any Paying Agent under the provisions of this Indenture shall, upon demand of the Company, be paid to the Trustee, or, if sufficient moneys have been deposited pursuant to Section 9.1, to the Company, and thereupon such Paying Agent shall be released from all further liability with respect to such moneys.

9.8. MONEYS HELD BY TRUSTEE.

Any moneys deposited with the Trustee or any Paying Agent or then held by the Company in trust for the payment of the principal of, or interest or premium, if any, on, any Security that are not applied but remain unclaimed by the Holder of such Security for two years after the date upon which the principal of, or interest or premium, if any, on, such Security shall have respectively become due and payable shall be repaid to the Company upon Company Request, or if such moneys are then held by the Company in trust, such moneys shall be released from such trust; and the Holder of such Security entitled to receive such payment shall thereafter, as an unsecured general creditor, look only to the Company for the payment thereof, and all liability of the Trustee or such Paying Agent with respect to such trust money shall thereupon cease; PROVIDED, HOWEVER, that the Trustee or any such Paying Agent, before being required to make any such repayment, may, at the expense of the Company, either mail to each Securityholder affected, at the address shown in the register of the Securities maintained by the Registrar, or cause to be published once a week for two successive weeks, in a newspaper published in the English language, customarily published each Business Day and of general circulation in the City of New York, New York, a notice that such money remains unclaimed and that, after a date specified therein, which shall not be less than 30 days from the date of such mailing or publication, any unclaimed balance of such moneys then remaining will be repaid to the Company. After payment to the Company or the release of any money held in trust by the Company, Securityholders entitled to the money must look only to the Company for payment as general creditors, unless applicable abandoned property law designates another Person.

ARTICLE 10 – MISCELLANEOUS

10.1. TRUST INDENTURE ACT CONTROLS.

If any provision of this Indenture limits, qualifies or conflicts with another provision which is required to be included in this Indenture by the TIA, the required provision shall control. If any provision of this Indenture modifies or excludes any provision of the TIA which may be so modified or excluded, the latter provision shall be deemed to apply to this Indenture as so modified or to be excluded, as the case may be.

10.2. NOTICES.

Any notice or communication shall be given in writing and delivered in Person, sent by facsimile (and receipt confirmed by telephone or electronic transmission report), delivered by commercial courier service or mailed by first-class mail, postage prepaid, addressed as follows:

If to the Company:

Aeglea BioTherapeutics, Inc.
901 S. MoPac Expressway
Barton Oaks Plaza One
Suite 250
Austin, TX 78746
Attention: Chief Financial Officer

Copy to:

Fenwick & West LLP
Silicon Valley Center
801 California Street
Mountain View, CA 94041
Fax: (650) 938-5200
Attention: Robert Freedman

If to the Trustee:

The Company or the Trustee by written notice to the other may designate additional or different addresses for subsequent notices or communications. Any notice or communication to the Company or the Trustee shall be deemed to have been given or made as of the date so delivered if personally delivered; when receipt is confirmed by telephone or electronic transmission report, if sent by facsimile; and three Business Days after mailing if sent by registered or certified mail, postage prepaid (except that a notice of change of address shall not be deemed to have been given until actually received by the addressee).

Any notice or communication mailed to a Securityholder shall be mailed to such Securityholder by first-class mail, postage prepaid, at such Securityholder's address shown on the register kept by the Registrar.

Failure to mail, or any defect in, a notice or communication to a Securityholder shall not affect its sufficiency with respect to other Securityholders. If a notice or communication to a Securityholder is mailed in the manner provided above, it shall be deemed duly given, three Business Days after such mailing, whether or not the addressee receives it.

In case by reason of the suspension of regular mail service, or by reason of any other cause, it shall be impossible to mail any notice as required by this Indenture, then such method of notification as shall be made with the approval of the Trustee shall constitute a sufficient mailing of such notice.

In the case of Global Securities, notices or communications to be given to Securityholders shall be given to the Depository, in accordance with its applicable policies as in effect from time to time.

In addition to the manner provided for in the foregoing provisions, notices or communications to Securityholders shall be given by the Company by release made to Reuters Economic Services and Bloomberg Business News.

10.3. COMMUNICATIONS BY HOLDERS WITH OTHER HOLDERS.

Securityholders of any Series may communicate pursuant to TIA Section 312(b) with other Securityholders of that Series or any other Series with respect to their rights under this Indenture or the Securities of that Series or any other Series. The Company, the Trustee, the Registrar and any other Person shall have the protection of TIA Section 312(c).

10.4. CERTIFICATE AND OPINION AS TO CONDITIONS PRECEDENT.

Upon any request or application by the Company to the Trustee to take any action under this Indenture, the Company shall furnish to the Trustee:

(1) an Officers' Certificate (which shall include the statements set forth in Section 10.5 below) stating that, in the opinion of the signers, all conditions precedent, if any, provided for in this Indenture relating to the proposed action have been complied with; and

(2) an Opinion of Counsel (which shall include the statements set forth in Section 10.5 below) stating that, in the opinion of such counsel, all such conditions precedent have been complied with.

10.5. STATEMENT REQUIRED IN CERTIFICATE AND OPINION.

Each certificate and opinion with respect to compliance with a condition or covenant provided for in this Indenture (other than pursuant to Section 4.4) shall include:

(1) a statement that the Person making such certificate or opinion has read such covenant or condition;

(2) a brief statement as to the nature and scope of the examination or investigation upon which the statements or opinions contained in such certificate or opinion are based;

(3) a statement that, in the opinion of such Person, it or he has made such examination or investigation as is necessary to enable it or him to express an informed opinion as to whether or not such covenant or condition has been complied with; and

(4) a statement as to whether or not, in the opinion of such Person, such covenant or condition has been complied with.

10.6. RULES BY TRUSTEE AND AGENTS.

The Trustee may make reasonable rules for action by or at meetings of Securityholders. The Registrar and Paying Agent may make reasonable rules for their functions.

10.7. BUSINESS DAYS; LEGAL HOLIDAYS; PLACE OF PAYMENT.

A "Business Day" is a day that is not a Legal Holiday. A "Legal Holiday" is a Saturday, a Sunday, a federally-recognized holiday or a day on which banking institutions are not authorized or required by law, regulation or executive order to be open in the State of New York.

If a payment date is a Legal Holiday at a Place of Payment, payment may be made at that place on the next succeeding day that is not a Legal Holiday, and no interest shall accrue for the intervening period. "Place of Payment" means the place or places where the principal of, and interest and premium, if any, on, the Securities of a Series are payable as specified as contemplated by Section 2.2. If the regular record date is a Legal Holiday, the record date shall not be affected.

10.8. GOVERNING LAW.

THIS INDENTURE AND THE SECURITIES SHALL BE GOVERNED BY AND CONSTRUED IN ACCORDANCE WITH THE LAWS OF THE STATE OF NEW YORK, AS APPLIED TO CONTRACTS MADE AND PERFORMED WITHIN THE STATE OF NEW YORK WITHOUT REGARD TO PRINCIPLES OF CONFLICTS OF LAW.

10.9. NO ADVERSE INTERPRETATION OF OTHER AGREEMENTS.

This Indenture may not be used to interpret another indenture, loan, security or debt agreement of the Company or any Subsidiary thereof. No such indenture, loan, security or debt agreement may be used to interpret this Indenture.

10.10. NO RECOURSE AGAINST OTHERS.

A director, officer, employee, stockholder or incorporator, as such, of the Company shall not have any liability for any obligations of the Company under the Securities or the Indenture. Each Securityholder by accepting a Security waives and releases all such liability. Such waiver and release are part of the consideration for the issuance of the Securities.

10.11. SUCCESSORS.

All covenants and agreements of the Company in this Indenture and the Securities shall bind the Company's successors and assigns, whether so expressed or not. All agreements of the Trustee, any additional trustee and any Paying Agents in this Indenture shall bind their respective successors and assigns.

10.12. MULTIPLE COUNTERPARTS.

The parties may sign multiple counterparts of this Indenture. Each signed counterpart shall be deemed an original, but all of them together represent one and the same agreement.

10.13. TABLE OF CONTENTS, HEADINGS, ETC.

The table of contents, cross-reference sheet and headings of the Articles and Sections of this Indenture have been inserted for convenience of reference only, are not to be considered a part hereof, and shall in no way modify or restrict any of the terms or provisions hereof.

10.14. SEVERABILITY.

Each provision of this Indenture shall be considered separable, and if for any reason any provision which is not essential to the effectuation of the basic purpose of this Indenture or the Securities shall be invalid, illegal or unenforceable, the validity, legality and enforceability of the remaining provisions shall not in any way be affected or impaired thereby, and a Holder shall have no claim therefor against any party hereto.

10.15. SECURITIES IN A FOREIGN CURRENCY OR IN EUROS.

Unless otherwise specified in a Board Resolution, a supplemental indenture hereto or an Officers' Certificate delivered pursuant to Section 2.2 with respect to a particular Series of Securities, whenever for purposes of this Indenture any action may be taken by the Holders of a specified percentage in aggregate principal amount of Securities of all Series or all Series affected by a particular action at the time outstanding and, at such time, there are outstanding Securities of any Series which are denominated in a coin or currency other than Dollars (including Euros), then the principal amount of Securities of such Series which shall be deemed to be outstanding for the purpose of taking such action shall be that amount of Dollars that could be obtained for such amount at the Market Exchange Rate at such time. For purposes of this Section 10.15, "Market Exchange Rate" shall mean the noon Dollar buying rate in New York City for cable transfers of that currency as published by the Federal Reserve Bank of New York; PROVIDED, HOWEVER, in the case of Euros, Market Exchange Rate shall mean the rate of exchange determined by the Commission of the European Union (or any successor thereto) as published in the Official Journal of the European Union (such publication or any successor publication, the "Journal"). If such Market Exchange Rate is not available for any reason with respect to such currency, the Trustee shall use, in its sole discretion and without liability on its part, such quotation of the Federal Reserve Bank of New York or, in the case of Euros, the rate of exchange as published in the Journal, as of the most recent available date, or quotations or, in the case of Euros, rates of

exchange from one or more major banks in New York City or in the country of issue of the currency in question or, in the case of Euros, in Luxembourg or such other quotations or, in the case of Euros, rates of exchange as the Trustee, upon consultation with the Company, shall deem appropriate. The provisions of this paragraph shall apply in determining the equivalent principal amount in respect of Securities of a Series denominated in currency other than Dollars in connection with any action taken by Holders of Securities pursuant to the terms of this Indenture.

All decisions and determinations of the Trustee regarding the Market Exchange Rate or any alternative determination provided for in the preceding paragraph shall be in the Trustee's sole discretion, and shall, in the absence of manifest error, be conclusive to the extent permitted by law for all purposes and irrevocably binding upon the Company and all Holders.

10.16. JUDGMENT CURRENCY.

The Company agrees, to the fullest extent that it may effectively do so under applicable law, that (a) if for the purpose of obtaining judgment in any court it is necessary to convert the sum due in respect of the principal of, or interest or premium, if any, or other amount on, the Securities of any Series (the "Required Currency") into a currency in which a judgment will be rendered (the "Judgment Currency"), the rate of exchange used shall be the rate at which, in accordance with normal banking procedures, the Trustee could purchase in The City of New York the Required Currency with the Judgment Currency on the day on which final unappealable judgment is entered, unless such day is not a Business Day, in which instance, the rate of exchange used shall be the rate at which, in accordance with normal banking procedures, the Trustee could purchase in The City of New York the Required Currency with the Judgment Currency on the Business Day preceding the day on which final unappealable judgment is entered and (b) its obligations under this Indenture to make payments in the Required Currency (i) shall not be discharged or satisfied by any tender or any recovery pursuant to any judgment (whether or not entered in accordance with subsection (a)) in any currency other than the Required Currency, except to the extent that such tender or recovery shall result in the actual receipt, by the payee, of the full amount of the Required Currency expressed to be payable in respect of such payments, (ii) shall be enforceable as an alternative or additional cause of action for the purpose of recovering in the Required Currency the amount, if any, by which such actual receipt shall fall short of the full amount of the Required Currency so expressed to be payable and (iii) shall not be affected by judgment being obtained for any other sum due under this Indenture.

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IN WITNESS WHEREOF, the parties hereto have caused this Indenture to be duly executed, and their respective corporate seals to be hereunto affixed and attested, all as of the day and year first above written.

AEGLEA BIOTHERAPEUTICS, INC.

By: _____
Name: _____
Title: _____

[Name of Trustee]

By: _____
Name: _____
Title: _____

By: _____
Name: _____
Title: _____



December 21, 2018

Aeglea BioTherapeutics, Inc.
901 S. MoPac Expressway
Barton Oaks Plaza Suite 250
Austin, TX 78746

Gentlemen/Ladies:

At your request, we have examined the Registration Statement on Form S-3 filed by Aeglea BioTherapeutics, Inc., a Delaware corporation (the "**Company**"), with the Securities and Exchange Commission (the "**Commission**") on December 21, 2018 (the "**Registration Statement**") in connection with the registration under the Securities Act of 1933, as amended (the "**Securities Act**"), of the offering and sale from time to time of (i) shares of the Company's common stock, \$0.0001 par value per share (the "**Common Stock**"), (ii) shares of the Company's preferred stock, \$0.0001 par value per share (the "**Preferred Stock**"), (iii) one or more series of debt securities (the "**Debt Securities**") issuable pursuant to an indenture (the "**Indenture**") by and between the Company and a financial institution to be identified therein as trustee (the "**Trustee**"), (iv) warrants to purchase Common Stock, Preferred Stock and/or Debt Securities (the "**Warrants**"), (v) subscription rights to purchase Common Stock, Preferred Stock and/or Debt Securities (the "**Subscription Rights**"), and/or (vi) units consisting of any combination of such foregoing securities described in clauses (i) through (v) above (the "**Units**"), having an aggregate public offering price of up to \$275,000,000. The Common Stock, the Preferred Stock, the Debt Securities, the Warrants, the Subscription Rights and the Units are collectively referred to herein as the "**Securities**." The Securities may be sold from time to time by the Company as set forth in the Registration Statement, the prospectus contained within the Registration Statement (the "**Prospectus**") and supplements to the Prospectus.

We advise you that we have also examined (i) the prospectus supplement filed, together with the Registration Statement and Prospectus, with the Commission on December 21, 2018 (the "**Prospectus Supplement**") relating to the sale by the Company through Jefferies LLC, as the sales agent (the "**Sales Agent**"), from time to time of shares of Common Stock (the "**Placement Shares**") having an aggregate maximum offering price of up to \$60,000,000 pursuant to the Registration Statement, the Prospectus and the Prospectus Supplement for the sale of the Placement Shares included in the Registration Statement, and (ii) that certain Open Market Sale AgreementSM, dated as of December 21, 2018, by and between the Company and the Sales Agent (the "**Sales Agreement**").

In connection with our opinion expressed below we have examined originals or copies of the Company's Restated Certificate of Incorporation (the "**Restated Certificate**") and Bylaws (the "**Bylaws**" and, together with the Restated Certificate, as each may be amended, modified or restated, the "**Charter Documents**"), certain corporate proceedings of the Company's board of directors (the "**Board**") and stockholders relating to the Registration Statement, the Company's Restated Certificate and Bylaws, and such other agreements, documents, certificates and statements of the Company, its transfer agent and public or government officials, as we have deemed advisable, and have examined such questions of law as we have considered necessary. We have assumed, and express no opinion as to, the genuineness of all signatures on documents submitted to us, the authenticity and completeness of all documents submitted to us as originals, the conformity to originals and completeness of all documents submitted to us as copies, the legal capacity of all persons or entities executing the same, the absence of any undisclosed termination, modification, waiver or amendment to any document reviewed by us, the absence of any other extrinsic agreements or documents that might change or affect the interpretation or terms of documents we have reviewed, and the due authorization, execution and delivery of all such documents where due authorization, execution and delivery are prerequisites to the effectiveness thereof. In giving our opinion, we have also relied upon a good standing certificate regarding the Company issued by the Delaware Secretary of State dated December 21, 2018 and a management certificate addressed to us and dated of even date herewith executed by the Company containing certain factual representations (the "**Management Certificate**").

We also have assumed that any certificates or instruments representing the Securities, including the Placement Shares, will be, when issued, properly signed by authorized officers of the Company, and, in the case of Debt Securities, properly authenticated in accordance with the terms of the Indenture and delivered to the intended recipients with the intent that the Company be bound thereby. Furthermore, with respect to the Company's uncertificated capital stock, we assume that issued Common Stock, including any Placement Shares, will not be reissued by the Company in uncertificated form until any previously issued stock certificate representing such issued Common Stock has been surrendered to the Company in accordance with Section 158 of the Delaware

General Corporation Law, and that the Company will properly register the transfer of the Common Stock to the purchasers of such Common Stock on the Company's record of uncertificated securities. We also have assumed that the Indenture at the time of execution, authentication, issuance and delivery of the Debt Securities will be a valid and legally binding obligation of the Trustee.

As to matters of fact relevant to this opinion, we have relied solely upon our examination of the documents referred to above and the Management Certificate and have assumed the current accuracy and completeness of the information obtained from the documents referred to above and the representations and warranties made by representatives of the Company to us, including but not limited to those set forth in the Management Certificate. We have made no independent investigation or other attempt to verify the accuracy of any of such information or to determine the existence or non-existence of any other factual matters.

We are admitted to practice law in the State of California, and we render this opinion only with respect to, and express no opinion herein concerning the application or effect of the laws of any jurisdiction other than (i) the existing laws of the State of California, (ii) the Delaware General Corporation Law, and (iii) solely with respect to whether or not the Debt Securities are the valid and binding obligations of the Company, the existing laws of the state of New York (clauses (i) through (iii) collectively, the "**Applicable Laws**"). To the extent that any Warrant Agreement, Subscription Rights Agreement or Unit Agreement (each as defined below) is governed by the laws of any jurisdiction other than the State of California, our opinion expressed below assumes that Internal California Law (as defined below) will exclusively apply to and govern such Warrant Agreement, Subscription Rights Agreement or Unit Agreement, without regard to any interpretation or construction that might be indicated by the laws stated as governing any such Warrant Agreement, Subscription Rights Agreement or Unit Agreement. As used herein "**Internal California Law**" means the internal laws of the State of California applicable to a contract made by California residents in the State of California that selects California law as the governing law of such contract, without regard to any laws or equitable principles regarding choice of law, conflict of laws or public policies that might make any other law(s) applicable. Without limitation, we express no opinion with respect to the federal laws of the United States of America or the securities or "blue sky" laws of any state or any local or regional laws.

In connection with our opinions expressed below, we have assumed that, (i) at or prior to the time of the delivery of any of the Securities, including the Placement Shares, there will not have occurred any change in the law or the facts affecting the validity of the Securities, (ii) if any Debt Securities are issued, such Debt Securities will only be issued pursuant to the Indenture in the form filed with the Registration Statement as an exhibit and that there will not have occurred any change in law affecting the enforceability of the Debt Securities or the Indenture, (iii) all applicable covenants binding on or applicable to the Company restricting the issuance of Debt Securities will have been validly waived, (iv) the Registration Statement and any amendments (including any necessary post-effective amendments) will have been declared effective under the Securities Act, (v) at the time of the offer, issuance and sale of any Securities, including the Placement Shares, no stop order suspending the Registration Statement's effectiveness will have been issued and remain in effect, (vi) no future amendments will be made to the Charter Documents that would be in conflict with or inconsistent with the Company's right and ability to issue the Securities, including without limitation the Placement Shares, (vii) at the time of each offer, issuance and sale of any Securities, including without limitation the Placement Shares, the Company will have a sufficient number of authorized and unissued and unreserved shares of the applicable class or series of its capital stock included in (or purchasable upon exercise or conversion of) the Securities, including without limitation the Placement Shares, so issued and sold (after taking into account all other outstanding securities of the Company which may require the Company to issue shares of such applicable class or series) to be able to issue all such shares, and (viii) all purchasers of Securities, including without limitation the purchasers of the Placement Shares, will timely pay in full to the Company all amounts they have agreed to pay to purchase such Securities, including the Placement Shares, as approved by the Board or a duly authorized committee thereof, and that the purchase price of any Securities, including the Placement Shares, that are shares of capital stock will not be less than the par value thereof. We also have assumed that the terms of any Debt Securities to be established subsequent to the date hereof, the issuance and delivery of Securities, including the Placement Shares, subsequent to the date hereof and the compliance by the Company with the terms of such Securities, including the Placement Shares, will not violate any applicable law (including, without limitation, any law relating to usury or similar laws) or result in a violation of any provision of any of the Charter Documents or of any instrument or agreement then binding upon the Company or any restriction imposed by any court or governmental body having jurisdiction over the Company.

This opinion is qualified by, and is subject to, and we render no opinion with respect to, the following limitations and exceptions to the enforceability of the Debt Securities:

- (1) The effect of the laws of bankruptcy, insolvency, reorganization, arrangement, moratorium, fraudulent conveyance, assignment for the benefit of creditors, and other similar laws now or hereinafter in effect relating to or affecting the rights and remedies of creditors, including the effect of statutory or other laws regarding fraudulent transfers or preferential transfers.

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- (2) The effect of general principles of equity and similar principles, including, without limitation, concepts of materiality, reasonableness, good faith and fair dealing, public policy and unconscionability, and the possible unavailability of specific performance, injunctive relief, or other equitable remedies, regardless of whether considered in a proceeding in equity or at law.
 - (3) The effect of laws relating to usury or permissible rates of interest for loans, forbearances or the use of money.

We express no opinion regarding the effectiveness of any waiver or stay, extension or of unknown future rights. Further, we express no opinion regarding the effect of provisions relating to indemnification, exculpation or contribution to the extent such provisions may be held unenforceable as contrary to federal or state securities laws or public policy.

The Company has informed us that the Company intends to issue the Securities, including without limitation the Placement Shares, from time to time on a delayed or continuous basis. This opinion is limited to the Applicable Laws, including the rules and regulations thereunder, as in effect on the date hereof. We are basing this opinion on our understanding that, prior to issuing any Securities, excluding the Placement Shares, in connection with the Registration Statement, the Company will advise us in writing of the terms thereof and other information material thereto, will afford us an opportunity to review the operative documents pursuant to which such Securities are to be issued (including the Registration Statement, the Prospectus and the applicable supplement to the Prospectus, as then in effect) and will file such supplement or amendment to this opinion (if any) as we may reasonably consider necessary or appropriate with respect to such Securities. However, we undertake no responsibility to monitor the Company's future compliance with applicable laws, rules or regulations of the Commission or other governmental body. In particular, except with respect to the Placement Shares, we assume that the Company will obtain the requisite approval of the Board and the requisite approval of its stockholders, if required by the laws of the State of Delaware and the Charter Documents, or if necessary because the Company does not have a sufficient number of authorized but unissued and unreserved shares of its capital stock at the time of issuance to comply with any Securities. Except with respect to the Placement Shares, we also assume the Company will timely file any and all supplements to the Registration Statement and Prospectus as are necessary to comply with applicable laws in effect from time to time and duly amend its Restated Certificate to increase the authorized number of shares of its capital stock as necessary if the number of such shares to be sold pursuant to the Registration Statement would cause the Company to issue more such shares than it has authorized and unissued and unreserved.

With respect to our opinion expressed in paragraph (7) below, we have assumed that, upon the issuance of any of the Placement Shares, the total number of shares of Common Stock issued and outstanding and reserved for future issuance will not exceed the total number of shares of Common Stock that the Company is then authorized to issue under its Certificate of Incorporation, as then in effect.

Based upon the foregoing, we are of the following opinion:

1. With respect to the shares of Common Stock registered pursuant to the Registration Statement, when (i) the issuance of and the terms of the offering of such shares of Common Stock and related matters have been duly authorized by all required corporate action of the Board or a duly authorized committee thereof, and, if required, of the stockholders of the Company in accordance with the Charter Documents and Applicable Laws and (ii) if required, certificates representing the shares of Common Stock have been duly executed, countersigned, registered and delivered either (a) in accordance with the applicable definitive purchase, underwriting or similar agreement approved by the Board, or upon the exercise of Warrants to purchase Common Stock, upon payment of the consideration therefor (in an amount not less than the par value of the Common Stock) provided for therein and approved by the Board or a duly authorized committee thereof, or (b) upon conversion or exercise of any other security of the Company, in accordance with the terms of such security or the instrument governing such security providing for such conversion or exercise as approved by the Board, for the consideration approved by the Board (in an amount not less than the par value per share of the Common Stock), then such shares of Common Stock will be validly issued, fully paid and nonassessable.

2. With respect to any particular series of shares of Preferred Stock registered pursuant to the Registration Statement, when (i) the issuance and terms of such shares of Preferred Stock, the terms of the offering thereof and related matters, including the adoption of a certificate of designation relating to such Preferred Stock conforming to the Company's Restated Certificate and Bylaws and the Delaware General Corporation Law (a "*Certificate*") and the filing of such Certificate with the Secretary of State of the State of Delaware (or the filing of an amendment to the Company's Certificate of Incorporation to similar effect), have been duly authorized by all required corporate action of the Board and, if required, of the stockholders of the Company in accordance with the Charter Documents and Applicable Laws and (ii) if required, certificates representing the shares of Preferred Stock have been duly executed, countersigned, registered and delivered either (a) in accordance with the applicable definitive purchase, underwriting or similar agreement approved by the Board, or upon the exercise of Warrants to purchase Preferred Stock, upon payment of the consideration therefor (in an amount not less than the par value per share of such Preferred Stock) provided for therein and approved by the Board or (b) upon conversion or exercise of any other security of the Company, in accordance with the terms of such security or the instrument governing such security providing for such conversion or exercise as approved by the Board, for the consideration approved by the Board (in an amount not less than the par value per share of the Preferred Stock), then such shares of Preferred Stock will be validly issued, fully paid and nonassessable.

3. With respect to any Debt Securities registered pursuant to the Registration Statement, when (i) the issuance of such Debt Securities has been duly authorized by all required corporate action of the Board and, if required, of the stockholders of the Company in accordance with the Charter Documents and Applicable Laws, (ii) an Indenture relating to such Debt Securities in the form filed with the Registration Statement as an exhibit has been duly authorized and validly executed and delivered by each of the Company (by duly authorized officers of the Company) and the Trustee, (iii) the form and terms of the Debt Securities have been duly established in accordance with the Indenture pursuant to resolutions duly adopted by the Board and as set forth in an officer's certificate or supplemental indenture duly authorized by the Board in accordance with the Charter Documents and Applicable Laws and duly executed by an authorized officer of the Company, and (iv) instruments representing such Debt Securities have been duly executed and authenticated in accordance with the terms of the Indenture and any supplement thereto, and issued, sold and delivered in the manner and for the consideration approved by the Board and stated in the Registration Statement, the Prospectus and any prospectus supplement relating thereto (as amended as of the date of such issuance, sale and delivery), any applicable definitive purchase, underwriting or similar agreement and upon the exercise of Warrants to purchase Debt Securities, upon payment of the consideration therefor provided for therein, then the Debt Securities will be validly issued and will constitute valid and binding obligations of the Company.

4. With respect to any Warrants registered pursuant to the Registration Statement, when (i) the issuance and terms of such Warrants, the terms, execution and delivery of the warrant agreement relating to the Warrants ("**Warrant Agreement**"), the terms of the offering thereof and related matters have been duly authorized by all required corporate action of the Board and, if required, of the stockholders of the Company in accordance with the Charter Documents and Applicable Laws, (ii) the Warrant Agreement has been duly authorized and validly executed and delivered by the Company by duly authorized officers of the Company, and (iii) such Warrants have been duly executed, issued and delivered by the Company by duly authorized officers of the Company in accordance with the provisions of the applicable Warrant Agreement and the applicable definitive purchase, underwriting or similar agreement approved by the Board, upon payment of the consideration therefor provided for therein and approved by the Board, such Warrants will constitute valid and binding obligations of the Company.

5. With respect to any Subscription Rights registered pursuant to the Registration Statement, when (i) the issuance and terms of such Subscription Rights, the terms, execution and delivery of the subscription rights agreement relating to the Subscription Rights ("**Subscription Rights Agreement**"), the terms of the offering thereof and related matters have been duly authorized by all required corporate action of the Board and, if required, the stockholders of the Company in accordance with the Charter Documents and Applicable Laws, (ii) the Subscription Rights Agreement has been duly authorized and validly executed and delivered, and (iii) such Subscription Rights have been duly executed, issued and delivered by the Company by duly authorized officers of the Company in accordance with the provisions of the applicable Subscription Rights Agreement and the applicable definitive purchase, underwriting or similar agreement approved by the Board, upon payment of the consideration therefor provided for therein and approved by the Board, such Subscription Rights will constitute valid and binding obligations of the Company.

6. With respect to any Units registered pursuant to the Registration Statement, when (i) the conditions outlined in the immediately preceding paragraphs (2) through (6) that apply to the Securities that make up such Units are all met, (ii) the issuance and terms of such Units, the terms, execution and delivery of the unit purchase agreement relating to such Units ("**Unit Agreement**"), the terms of the offering thereof and related matters have been duly authorized by all required corporate action of the Board and, if required, of the stockholders of the Company, (iii) the Unit Agreement has been duly authorized and validly executed and delivered by the Company by duly authorized officers of the Company, and (iv) such Units have been duly executed, issued and delivered by the Company by duly authorized officers of the Company in accordance with the provisions of the applicable Unit Agreement and the applicable definitive purchase, underwriting or similar agreement approved by the Board, upon payment of the consideration therefor provided for therein and approved by the Board, such Units will constitute valid and binding obligations of the Company.

7. The Placement Shares, to be issued and sold by the Company, when issued, sold and delivered in the manner of and for consideration (of not less than par value per share of the Common Stock) in the manner contemplated by the Sales Agreement and in accordance with the resolutions duly adopted and to be duly adopted by the Board and to be duly adopted by the Placement Committee of the Board with respect to the offer, sale and issuance of the Placement Shares, will be validly issued, fully paid and nonassessable.

We consent to the use of this opinion as an exhibit to the Registration Statement and further consent to all references to us, if any, in the Registration Statement, the Prospectus constituting a part thereof and any amendments thereto. In giving this consent we do not thereby admit that we come within the category of persons whose consent is required by the Securities Act or by the rules and regulations promulgated thereunder.

[Concluding Paragraph Follows on Next Page]

This opinion is intended solely for use in connection with the issuance and sale of the Securities subject to the Registration Statement and is not to be relied upon for any other purpose. In providing this letter, we are opining only as to the specific legal issues expressly set forth above, and no opinion shall be inferred as to any other matter or matters. This opinion is rendered on, and speaks only as of, the date of this letter first written above, is based solely on our understanding of facts in existence as of such date after the aforementioned examination and does not address any potential changes in facts, circumstance or law that may occur after the date of this opinion letter. We assume no obligation to advise you of any fact, circumstance, event or change in the law or the facts that may hereafter be brought to our attention whether or not such occurrence would affect or modify any of the opinions expressed herein.

Very truly yours,

/s/ Fenwick & West LLP
Fenwick & West LLP

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of Aeglea BioTherapeutics, Inc. of our report dated March 13, 2018 relating to the financial statements, which appears in Aeglea BioTherapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2017. We also consent to the reference to us under the heading "Experts," in such Registration Statement.

/s/ PricewaterhouseCoopers LLP

Austin, TX
December 21, 2018