Table of Contents

Filed Pursuant to Rule 424(b)(4)
Registration No. 333-224303

PROSPECTUS

5,500,000 Shares

Common Stock

$25.50 per share

We are offering 5,500,000 shares of our common stock in this offering. Our common stock is listed on the Nasdaq Global Select Market under the symbol "APLS." The last reported sale price of our common stock on the Nasdaq Global Select Market on April 18, 2018 was $26.37 per share.

Investing in our common stock involves risks. See "Risk Factors" beginning on page 11.

We are an "emerging growth company" under applicable Securities and Exchange Commission rules and, as such, have elected to comply with certain reduced public company disclosure requirements. See "Summary—Implications of Being an Emerging Growth Company."

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

	Per Share	Total
Public Offering Price	$ 25.50	$140,250,000
Underwriting Discounts and Commissions(1)	$ 1.53	$ 8,415,000
Proceeds to us (before expenses)	$ 23.97	$131,835,000

(1) We refer you to "Underwriting" beginning on page 163 for additional information regarding underwriter compensation.

The underwriters also have the option to purchase up to an additional 825,000 shares of our common stock on the same terms and conditions set forth above for 30 days after the date of this prospectus.

The underwriters expect to deliver the shares to purchasers on or about April 23, 2018.

Citigroup **J.P. Morgan** **Cowen**

April 18, 2018.

TABLE OF CONTENTS

We have not authorized anyone to provide you with different information, and we take no responsibility for any other information others may give you. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the front of this prospectus.

No action is being taken in any jurisdiction outside the United States to permit a public offering of our common stock or possession or distribution of this prospectus in that jurisdiction. Persons who come into possession of this prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus applicable to that jurisdiction.

SUMMARY

This summary highlights, and is qualified in its entirety by, the more detailed information and consolidated financial statements included elsewhere in this prospectus. This summary does not contain all of the information that may be important to you. You should read and carefully consider the entire prospectus, especially our consolidated financial statements and the related notes thereto appearing at the end of this prospectus and the "Risk Factors" section of this prospectus, before deciding to invest in our common stock.

Overview

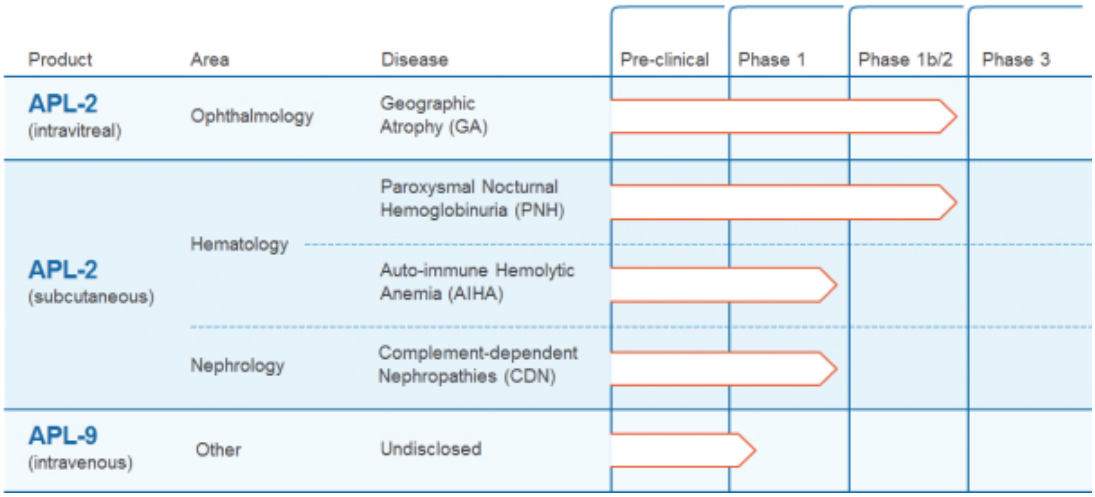
We are a clinical-stage biopharmaceutical company focused on the development of novel therapeutic compounds to treat disease through the inhibition of the complement system, which is an integral component of the immune system, at the level of C3, the central protein in the complement cascade. We believe that this approach can result in broad inhibition of the principal pathways of the complement system and has the potential to effectively control a broad array of complement-dependent autoimmune and inflammatory diseases.

We have the most advanced clinical program targeting C3. We believe that our lead product candidate, APL-2, has the potential to be a best-in-class treatment that may address the limitations of existing treatment options or provide a treatment option where there currently is none. APL-2 has already shown activity that we believe is clinically meaningful in clinical trials for two distinct medical conditions—geographic atrophy in age-related macular degeneration, or GA, and paroxysmal nocturnal hemoglobinuria, or PNH—and we plan to conduct clinical trials in additional complement-dependent diseases. In our Phase 2 clinical trial of APL-2 in patients with GA, treatment with APL-2 resulted in a significant reduction in the rate of GA lesion growth over 12 months, and we are planning to initiate a Phase 3 clinical program evaluating APL-2 in patients with GA. In our two ongoing Phase 1b clinical trials in PNH, APL-2 achieved improvements in transfusion dependency, hemoglobin levels and other hematological indicators that we believe are clinically meaningful. We are also developing other novel compounds targeting C3. We hold worldwide commercialization rights to APL-2 and these other novel compounds targeting C3.

Our Programs

Our lead product candidate, APL-2, is a C3 inhibitor. APL-2 is a conjugate of a compstatin analogue, formulated both for intravitreal injection, which is an injection directly into the eye, and systemic administration by subcutaneous injection, which is an injection into the tissue under the skin.

The following table summarizes key information about our clinical programs:



Geographic Atrophy

In GA, we are developing APL-2 to be injected intravitreally as a monotherapy. GA is an advanced form of age-related macular degeneration, or AMD, which is a disorder of the central portion of the retina characterized by progressive retinal cell death that ultimately leads to blindness. GA is a disease with significant unmet need that affects approximately one million patients in the United States and for which there are no U.S. Food and Drug Administration, or FDA, approved therapies. In August 2017, we completed the primary endpoint analysis for the 12-month treatment period in our Phase 2 clinical trial in 246 patients with GA, and in February 2018 we completed our analysis of the results for the six-month period following the 12-month treatment period during which patients were monitored and did not receive APL-2.

In the Phase 2 trial, APL-2 achieved the primary endpoint of reduction in the rate of GA lesion growth at 12 months. Patients treated monthly with APL-2 showed a 29% reduction in the rate of GA lesion growth compared to sham, with a p-value of 0.008, and patients treated with APL-2 every other month showed a 20% reduction, with a p-value of 0.067. P-value is a conventional statistical method for measuring the statistical significance of clinical results. In our Phase 2 trial, we set statistical significance as a p-value of 0.1 or less, meaning that there is a 1-in-10 or less statistical probability that the observed results occurred by chance rather than as a result of a treatment effect. Because the p-value of these results was less than 0.1, they are statistically significant.

Additionally, in a *post hoc* analysis of the Phase 2 trial, a greater effect was observed during the second six months of the treatment period compared to the first six months. During the second six months, we observed a reduction in the rate of GA lesion growth for patients for whom images were available at six and 12 months of 47% with monthly administration compared to sham, with a p-value of less than 0.001, and a reduction of 33% with administration every other month compared to sham, with a p-value of 0.01. These results are also statistically significant.

After the 12-month treatment period, patients were monitored for a further six months without treatment. During this monitoring period, the GA lesions in the previously treated groups grew at a rate similar to sham. Patients who received monthly APL-2, and for whom images were available at 12 and 18 months, showed

only a 12% reduction in the growth rate of lesions over the six-month monitoring period compared to sham, while patients who received every other month administration of APL-2 showed a 9% reduction in the growth rate compared to sham. These differences are not considered to be statistically significant.

The most frequently reported adverse events in the trial were associated with the injection procedure and are common for intravitreal injections. In addition, during the 12-month treatment period and the six-month monitoring period (18 months total), we observed a higher incidence of new onset exudation, or fluid leakage in the retinas of eyes in which exudation had not previously been observed, in the study eyes treated with APL-2 as compared to sham, predominantly in patients with a history of wet AMD in the non-study eye, or fellow eye. Specifically, we observed that, after the 12-month treatment period and the six-month monitoring period, 21% of patients who received administration of APL-2 every month and 9% of patients who received administration of APL-2 every other month showed new onset exudation in the study eye, as compared to 1% in the sham group. We submitted a safety report to the FDA in April 2017 regarding these events, and the FDA has not communicated any concern or requested additional information with regards to these findings. Patients who experienced new onset exudation in the study eye were discontinued from treatment with APL-2 and were treated with standard-of-care therapies that inhibit vascular endothelial growth factor, or VEGF, a naturally occurring protein in the body that causes the growth of abnormal blood vessels and leakage in the eye. There was no meaningful negative impact on visual acuity resulting from the new onset exudations.

Following discussions with the FDA and the EMA, we have finalized the trial design for a Phase 3 clinical program to evaluate APL-2 for the treatment of GA. The Phase 3 program, which we plan to begin in the second half of 2018, will consist of two identical 600-patient prospective, multicenter, randomized, double-masked, sham-injection controlled clinical trials to assess the efficacy and safety of multiple intravitreal injections of APL-2 in patients with GA. The Phase 3 clinical trials will be similar in design to the Phase 2 trial, including the eligibility criteria and primary endpoint of GA lesion growth, except that patients will be treated with APL-2 for 24 months in the Phase 3 trials and there will not be a monitoring period. Additionally, unlike the Phase 2 trial, patients who develop new onset exudation in the study eye will continue to be treated with APL-2 along with VEGF injections, the current standard of care for wet AMD.

We also plan to initiate a Phase 1b/2, multi-center, open label clinical trial to evaluate the safety of intravitreal APL-2 therapy when administered in parallel with anti-VEGF treatments in patients with wet AMD in the study eye in the second quarter of 2018. In this trial, we will evaluate whether treatment with APL-2 may allow wet AMD patients to reduce their dependence on anti-VEGF treatments. We believe that the data from this trial may support the use of APL-2 in eyes afflicted with both wet AMD and GA.

Paroxysmal Nocturnal Hemoglobinuria

In PNH, we are developing APL-2 to be injected subcutaneously as a monotherapy. PNH is a rare, life-threatening, chronic, debilitating blood disorder characterized by the absence of certain proteins that normally regulate complement activity on the surface of blood cells. As a consequence, patients with PNH suffer from significant and chronic red blood cell loss, or hemolysis. The only therapy currently approved for the treatment of PNH, eculizumab (Soliris), inhibits the complement system by targeting C5, a protein that is downstream from C3 in the complement cascade. Inhibitors that target C5 are limited to addressing only one of the two mechanisms of hemolysis in PNH. Consequently, many patients with PNH who are on treatment with eculizumab remain anemic and continue to require frequent transfusions, conditions associated with a poor quality of life. By contrast, APL-2, because it targets C3, addresses both mechanisms of hemolysis and, we believe, may therefore significantly ameliorate these conditions.

In our ongoing Phase 1b clinical trials of APL-2 for the treatment of PNH, treatment with APL-2 has been associated with improvements in transfusion dependency, levels of hemoglobin—the protein that carries oxygen

from the lungs to the tissues of the body—and other hematological indicators that we believe are clinically meaningful. We made these observations both in patients who had not been treated with eculizumab, who we refer to as treatment-naïve patients, and in patients being treated with eculizumab who remained anemic and required frequent blood transfusions. In these trials, APL-2 has been generally well tolerated.

As of February 28, 2018, four of the six patients who had been treated with daily doses of 270 mg of APL-2 and with eculizumab remain on treatment in the trial, having received treatment with APL-2 for a total of between 16 and 19 months. Due to the response observed with the APL-2 treatment for each of the four remaining patients, the treating physicians have individually taken the decision either to reduce the dose of eculizumab to the label dose for patients who had received a higher dose of eculizumab or to withdraw eculizumab treatment. We intend to report additional data from these patients in the second quarter of 2018.

Additionally, we initiated enrollment of additional treatment-naive patients in our Phase 1b clinical trial in the first quarter of 2018. In April 2018, we reported interim results as of April 13, 2018 from eight treatment-naive patients in the trial who had completed the initial 28-day treatment period with a daily dose of 270 mg of APL-2. The reported patients had a mean lactate dehydrogenase, or LDH, of 11.6 times the upper limit of normal at baseline which was reduced to a mean LDH of 0.9 times the upper limit of normal at day 28. In addition, seven of the eight patients were below the upper limit of normal at day 28. These reported patients had an average increase in hemoglobin of 4.3 g/dL from a baseline average of 7.9 g/dL to an average last measurement of 12.2 g/dL within the first 12 weeks of the treatment period. Except for two patients, each of whom received a single transfusion within the first two weeks of treatment with APL-2, no other transfusions have been reported in this trial for any patients during the treatment period. APL-2 has generally been well tolerated in the reported patients. We plan to continue enrolling treatment-naive patients in this trial and plan to report additional data in June 2018.

We plan to initiate a Phase 3 clinical trial in patients with PNH comparing treatment with APL-2 to treatment with eculizumab as a monotherapy in the second half of 2018. We plan to enroll up to 70 patients with PNH in this trial who are then receiving eculizumab. The treatment period of the trial will consist of three parts: a four-week run-in period, a 16-week randomized treatment period and a 32-week open-label APL-2 only period. During the run-in period, all patients will receive twice-weekly subcutaneous doses of 1,080 mg of APL-2 in addition to patients' then current dose of eculizumab. The run-in period is designed to provide patients with sufficient plasma concentration of APL-2 to provide for what we expect to be adequate complement inhibition before withdrawing eculizumab. Following completion of the run-in period, patients will receive either 1,080mg of APL-2 twice per week or their current dose of eculizumab through the duration of the 16-week randomized treatment period. We expect that the primary endpoint will be the week 16 change from baseline in hemoglobin level. Following completion of the randomized treatment period, all patients will receive APL-2 only for 32 weeks in the open-label part.

We are currently discussing with the FDA, the European Medicines Agency, or EMA, and the Japanese Pharmaceuticals and Medical Devices Agency, or PMDA, the trial program that we will need to conduct to submit APL-2 for regulatory approval for PNH.

In April 2014, we received orphan drug designation from the FDA for APL-2 for PNH, and in December 2016 we received fast track designation from the FDA for APL-2 for PNH. If our clinical development of APL-2 for PNH is successful, we believe that APL-2 could be a best-in-class therapy for PNH, differentiated by mechanism, and has the potential to significantly increase the quality of life of patients with PNH as compared to the current standard of care.

Other Indications

We plan to initiate Phase 2 clinical trials of APL-2 in patients with autoimmune hemolytic anemia, or AIHA, in the first half of 2018, and in patients with complement-dependent kidney diseases, or nephropathies, in the first half of 2018. We plan to report data from the patients with AIHA in the second quarter of 2018 and from the patients with complement-dependent nephropathies in the second half of 2018.

By combining our core expertise in complement inhibition with our deep understanding of complement immunology, we intend to expand our pipeline of potential treatment areas with APL-2 and with additional new product candidates, including APL-9, which we are developing for intravenous administration in systemic indications.

Strategy

We aim to become a leading biopharmaceutical company focused on the discovery, development and commercialization of therapeutics to treat autoimmune and inflammatory diseases through complement inhibition. To achieve this goal, we are pursuing the following strategies:

- advance APL-2 (intravitreal administration) into Phase 3 clinical development in GA and Phase 1b/2 clinical development in wet AMD;
- advance APL-2 (systemic administration) into Phase 3 clinical development in PNH;
- expand APL-2 (systemic administration) into new indications with demonstrated complement involvement;
- expand our pipeline by developing new compounds and programs for other complement-dependent diseases;
- develop a custom drug delivery system for systemic administration of APL-2; and
- prepare for commercialization of APL-2.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the “Risk Factors” section of this prospectus immediately following this prospectus summary. These risks include the following:

- We have incurred significant losses since inception, expect to incur significant and increasing losses for at least the next several years, and may never achieve or maintain profitability.
- We will need substantial additional funding, including to complete our planned Phase 3 trials for APL-2. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- There are no approved therapies that act by inhibiting C3 and we may not be able to successfully develop and commercialize APL-2 or other product candidates.
- We are dependent on the successful development and commercialization of APL-2.
- If clinical trials of our product candidates fail to satisfactorily demonstrate safety and efficacy to the FDA and other regulators, we, or any future collaborators, may incur additional costs, experience delays or be unable to complete the development and commercialization of these product candidates.

- If a significant number of patients develop new onset exudations in our clinical trials of APL-2 in GA, we may need to limit the development of intravitreal APL-2 to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective.
- Given the severe and life-threatening nature of PNH, that many patients are on treatment with eculizumab and that patients and their physicians may be reluctant to forgo, discontinue or otherwise alter their existing therapy, we may encounter difficulty in recruiting a sufficient number of patients for our PNH trials. The small population of patients, competition for these patients, including with other companies conducting clinical trials of therapies for PNH, the nature of the disease and limited trial sites that support PNH treatment may make it difficult for us to enroll enough patients to complete our clinical trials of APL-2 in PNH in a timely and cost-effective manner.
- We rely on third parties to conduct our clinical trials and to manufacture and distribute our product candidates for our clinical trials. If these third parties do not perform satisfactorily, our development or commercialization efforts could be delayed or impaired.
- We may seek to establish collaborations and, if we are not able to establish or maintain them on commercially reasonable terms, we may have to alter our development and commercialization plans.
- If we fail to comply with our obligations under our license agreements with the Trustees of the University of Pennsylvania or any future intellectual property licenses with third parties, we could lose license rights that are important to our business.
- Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time consuming and uncertain and may prevent us or any future collaborators from obtaining approvals for the commercialization of some or all of our product candidates.

Our Corporate Information

We were incorporated under the laws of the State of Delaware on September 25, 2009 under the name Apellis Pharmaceuticals, Inc. Our principal executive offices are located at 6400 Westwind Way, Suite A, Crestwood, Kentucky 40014, and our telephone number is (502) 241-4114. Our website address is www.apellis.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

Except as otherwise indicated herein or as the context otherwise requires, references in this prospectus to “Apellis,” “the company,” “we,” “us” and “our” refer to Apellis Pharmaceuticals, Inc. and our wholly-owned subsidiary Apellis Australia Pty Ltd.

The Apellis logo is our trademark. The other trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners.

Implications of Being an Emerging Growth Company

As a company with less than $1.07 billion of revenue during our last fiscal year, we qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We may remain an emerging growth company until the last day of 2022, or until such earlier time as we have more than $1.07 billion in annual revenue, the market value of our stock held by non-affiliates is more than $700 million or we issue more than $1 billion of non-convertible debt over a three-year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure and other requirements that are applicable to other public companies that are not emerging growth companies. In particular,

in this prospectus, we have not included all of the executive compensation-related information that would be required if we were not an emerging growth company. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

THE OFFERING

Common stock offered by us	5,500,000 shares
Option to purchase additional shares	We have granted the underwriters an option for a period of 30 days from the date of this prospectus to purchase 825,000 additional shares of common stock.
Common stock to be outstanding immediately following this offering	55,872,762 shares (or 56,697,762 shares if the underwriters exercise their option to purchase additional shares in full)
Use of proceeds	We estimate that the net proceeds to us from this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, will be $131.3 million, or $151.1 million if the underwriters exercise their option to purchase additional shares in full. We intend to use the net proceeds from this offering, together with our existing cash and cash equivalents, to fund clinical development of APL-2 and to conduct research activities. The remainder will be used for working capital and other general corporate purposes. See the "Use of Proceeds" section in this prospectus for a more complete description of the intended use of proceeds from this offering.
Risk factors	You should read the "Risk Factors" section of this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Nasdaq Global Select Market symbol	"APLS"

The number of shares of our common stock to be outstanding after this offering is based on 50,372,762 shares of our common stock outstanding as of February 28, 2018 and excludes:

- 7,396,674 shares of our common stock issuable upon the exercise of stock options outstanding as of February 28, 2018, at a weighted-average exercise price of $6.33 per share;
- 2,078,522 and 972,164 additional shares of our common stock available for future issuance, as of February 28, 2018, under our 2017 stock incentive plan and our 2017 employee stock purchase plan, respectively as well as any automatic increases in the number of shares of common stock reserved under these plans; and
- 14,064 shares of our common stock issuable upon the exercise of warrants outstanding as of February 28, 2018, at an exercise price of $5.484 per share.

Unless otherwise indicated, all information in this prospectus assumes:

- no exercise of the outstanding options or warrants described above; and
- no exercise by the underwriters of their option to purchase up to 825,000 additional shares.

SUMMARY CONSOLIDATED FINANCIAL INFORMATION

You should read the following summary consolidated financial data together with our consolidated financial statements and the related notes appearing at the end of this prospectus and the "Selected Consolidated Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of this prospectus. We have derived the statement of operations data for the years ended December 31, 2015, 2016 and 2017 from our audited consolidated financial statements appearing at the end of this prospectus. In the opinion of management, the unaudited condensed consolidated financial data reflects all adjustments, consisting only of normal recurring adjustments, necessary for a fair presentation of the financial information as of and for the periods presented. Our historical results are not necessarily indicative of results that should be expected in any future period.

	Year Ended December 31,		
	2015	2016	2017
Consolidated Statement of Operations Data:			
Operating expenses:			
Research and development	$ 13,730,311	$ 22,978,599	$ 40,303,878
Cost of acquired in-process research and development	26,486,000	—	—
General and administrative	6,356,782	4,303,743	10,463,151
Operating loss	(46,573,093)	(27,282,342)	(50,767,029)
Loss from remeasurement of fair value of warrant	—	—	(153,692)
Interest income (expense), net(1)	50,853	135,309	(96,915)
Other income, net	6,284	22,396	11,542
Net loss and comprehensive loss	$ (46,515,956)	$ (27,124,637)	$ (51,006,094)
Net loss per common share, basic and diluted(2)	$ (8.03)	$ (3.22)	$ (3.68)
Weighted-average number of common shares used in net loss per share, basic and diluted(2)	5,795,040	8,428,366	13,870,949

(1) Includes amortization of debt discount associated with term loan facility and promissory note due to the issuance of warrants. See Notes 6 and 7 to our audited consolidated financial statements included elsewhere in this prospectus.

(2) See Note 13 in the notes to our audited consolidated financial statements appearing at the end of this prospectus for a description of the method used to calculate basic and diluted net loss per common share.

The following table sets forth summary consolidated balance sheet data as of December 31, 2017 on:

- an actual basis; and
- an as adjusted basis to give effect to our issuance and sale of 5,500,000 shares of common stock in this offering at a public offering price of $25.50 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

	As of December 31, 2017	
	Actual	As Adjusted
Consolidated Balance Sheet Data:		
Cash and cash equivalents	$ 175,643,529	$ 306,978,529
Working capital	175,461,348	306,796,348
Total assets	182,131,456	313,466,456
Term loan facility	19,806,944	19,806,944
Promissory note related party	6,583,402	6,583,402
Total liabilities	33,188,596	33,188,596
Convertible preferred stock	—	—
Accumulated deficit	(149,263,653)	(149,263,653)
Total stockholders' equity	148,942,860	280,277,860

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before you decide to invest in our common stock, you should carefully consider the risks described below, together with the other information contained in this prospectus, including our consolidated financial statements and the related notes appearing at the end of this prospectus. If any of the following risks actually occur, our business, financial condition, results of operations and future growth prospects could be harmed. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since inception, expect to incur significant and increasing losses for at least the next several years, and may never achieve or maintain profitability.

We have incurred significant annual net operating losses in every year since our inception. We expect to continue to incur significant and increasing net operating losses for at least the next several years. Our net losses were $46.5 million, $27.1 million and $51.0 million for the years ended December 31, 2015, 2016 and 2017, respectively. As of December 31, 2017, we had an accumulated deficit of $149.3 million. We have not generated any revenues from product sales, have not completed the development of any product candidate and may never have a product candidate approved for commercialization. We have financed our operations to date primarily through the sale of our common stock in our initial public offering and through private placements of our preferred stock. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and our clinical trials. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue to develop and conduct clinical trials in our current and new indications with our lead product candidate, APL-2;
- initiate and continue research and preclinical and clinical development efforts for any future product candidates;
- seek to identify and develop additional product candidates for complement-dependent diseases;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical trials, if any;
- establish sales, marketing, distribution and other commercial infrastructure in the future to commercialize any products for which we may obtain marketing approval;
- require the manufacture of larger quantities of product candidates for clinical development and, potentially, commercialization;
- maintain, expand and protect our intellectual property portfolio;
- hire and retain additional personnel, such as clinical, quality control and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and help us comply with our obligations as a public company; and
- add equipment and physical infrastructure to support our research and development programs.

Our ability to become and remain profitable depends on our ability to generate revenue. We do not expect to generate significant revenue unless and until we are, or any future collaborator is, able to obtain marketing

approval for, and successfully commercialize, one or more of our product candidates. Successful commercialization will require achievement of key milestones, including completing clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products for which we, or any of our future collaborators, may obtain marketing approval, satisfying any post-marketing requirements and obtaining reimbursement for our products from private insurance or government payors. Because of the uncertainties and risks associated with these activities, we are unable to accurately predict the timing and amount of revenues, and if or when we might achieve profitability. We and any future collaborators may never succeed in these activities and, even if we do, or any future collaborators do, we may never generate revenues that are large enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates or continue our operations. A decline in the value of our company could cause you to lose all or part of your investment.

We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.

As of December 31, 2017, we had cash and cash equivalents of $175.6 million. We do not believe that those cash and cash equivalents will be sufficient to enable us to fund our current operations for longer than 12 months from the date of this prospectus and have therefore concluded that this circumstance raises substantial doubt about our ability to continue as a going concern. See Note 1 to our consolidated financial statements appearing elsewhere in this prospectus for additional information on our assessment. If we are unable to raise sufficient capital in this offering or otherwise when needed, our business, financial condition and results of operations will be materially and adversely affected, and we will need to significantly modify our operational plans to continue as a going concern. If we are unable to continue as a going concern, we might have to liquidate our assets and the values we receive for our assets in liquidation or dissolution could be significantly lower than the values reflected in our financial statements. Our lack of cash resources and our conclusion that we may be unable to continue as a going concern may materially adversely affect our share price and our ability to raise new capital or to enter into critical contractual relations with third parties.

We have a limited operating history and no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.

We commenced operations in May 2010. Our operations to date have been limited to financing and staffing our company, developing our technology and conducting preclinical research and Phase 1 and Phase 2 clinical trials for our product candidates. We have not yet demonstrated an ability to successfully conduct Phase 3 clinical trials, obtain marketing approvals, manufacture a commercial-scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Accordingly, you should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by companies in the early stages of development, especially clinical-stage biopharmaceutical companies such as ours. Any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will eventually need to transition from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

We will need substantial additional funding, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. We have consumed substantial amounts of cash since our inception. For example, in the years ended December 31, 2015, 2016 and 2017, we used net cash of $18.9 million, $26.0 million and $46.6 million, respectively, in our operating activities substantially all of which related to research and development activities. As of December 31, 2017, our cash and cash equivalents were $175.6 million. We expect our expenses to increase in connection with our ongoing activities, particularly as we initiate new clinical trials of, initiate new research and preclinical development efforts for and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we may incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of a future collaborator. Furthermore, we expect to incur significant additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we may be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We plan to use the net proceeds of this offering primarily to fund clinical development of APL-2, to conduct research activities and for working capital and other general corporate purposes. We will be required to expend significant funds in order to advance the development of APL-2 in multiple disease areas, as well as other product candidates we may seek to develop. In addition, while we may seek one or more collaborators for future development of our product candidates for one or more indications, we may not be able to enter into a collaboration for any of our product candidates for such indications on suitable terms, on a timely basis or at all. In any event, the net proceeds of this offering, together with our existing cash and cash equivalents as of December 31, 2017, will not be sufficient to complete our planned Phase 3 clinical trials of APL-2 or to complete development of APL-2 or any of our other product candidates. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources to achieve our business objectives. We do not have any committed external source of funds. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents as of December 31, 2017, will enable us to fund our operating expenses and capital expenditure requirements at least into the third quarter of 2019. Our estimate as to how long we expect the net proceeds from this offering, together with our existing cash and cash equivalents, to be able to continue to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. Our future funding requirements, both short-term and long-term, will depend on many factors, including:

- the scope, progress, timing, costs and results of clinical trials of, and research and preclinical development efforts for, APL-2 and future product candidates;
- our ability to identify a collaborator for any of our product candidates and the terms and timing of any collaboration agreement that we may establish for the development and any commercialization of such product candidates;
- the number and characteristics of future product candidates that we pursue and their development requirements;
- the outcome, timing and costs of clinical trials and of seeking regulatory approvals;

- the costs of commercialization activities for any of our product candidates that receive marketing approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- subject to receipt of marketing approval, revenue, if any, received from commercial sales of our current and future product candidates;
- our headcount growth and associated costs as we expand our research and development and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims;
- the effect of competing technological and market developments;
- our ability to obtain adequate reimbursement for any product we commercialize; and
- the costs of operating as a public company.

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

We expect our expenses to increase in connection with our planned operations. To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, your ownership interest may be diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect your rights as a common stockholder. In addition, debt financing, if available, would result in fixed payment obligations and may involve agreements that include grants of security interests on our assets and restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, creating liens, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business.

For example, in connection with our term loan facility with Silicon Valley Bank, we granted a security interest on all of our assets, excluding our intellectual property, and agreed to a negative pledge on our intellectual property. We have agreed to grant a security interest on our interest in our licenses from the Trustees of the University of Pennsylvania, or Penn, if Penn consents to such security interest. The term loan facility also contains restrictive covenants including, subject to certain exceptions, covenants that prohibit us from transferring all or any part of our business or property, changing our business, liquidating or dissolving, merging with or acquiring another entity, entering into a transaction that will result in a change of control, incurring additional indebtedness, creating any lien on our property, paying dividends or redeeming stock, making payments on subordinated debt or entering into material transactions with affiliates. Future debt securities or other financing arrangements could contain similar or more restrictive negative covenants. We also would be required to obtain the consent of the holder of our promissory note to increase or extend the maturity of the term loan facility with Silicon Valley Bank. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

If we raise additional funds through collaborations or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to the Discovery, Development and Commercialization of Our Product Candidates

There are no approved therapies that act by inhibiting C3, and we may not be able to successfully develop and commercialize APL-2 or other product candidates.

APL-2 is a novel therapeutic compound and its potential benefit in controlling autoimmune and inflammatory diseases has not been established. APL-2 is designed to control disease through inhibition of C3. There are no approved therapies that act by inhibiting C3 and only one approved therapy that acts by inhibiting the complement system. As a result, APL-2 may not demonstrate in patients any or all of the pharmacological benefits we believe it may possess. We have not yet demonstrated efficacy and safety for APL-2 or any other product candidates in a pivotal trial or obtained marketing approval of any product candidate. We have evaluated APL-2 in preclinical studies and in clinical trials, including a Phase 2 clinical trial in geographic atrophy, or GA, but we have not yet advanced APL-2 into Phase 3 clinical development and we have not obtained regulatory approval to sell any product based on our therapeutic approaches.

If we are unsuccessful in our development efforts, we may not be able to advance the development of APL-2 or any other product candidate, commercialize products, raise capital, expand our business or continue our operations.

We are dependent on the successful development and commercialization of our lead product candidate, APL-2. If we are unable to develop, obtain marketing approval for or successfully commercialize this product candidate, either alone or through a collaboration, or if we experience significant delays in doing so, our business could be harmed.

We currently have no products approved for sale and are investing a significant portion of our efforts and financial resources to fund the development of APL-2. Our prospects are substantially dependent on our ability, or that of any future collaborator, to develop, obtain marketing approval for and successfully commercialize APL-2 in one or more disease indications.

The success of APL-2 will depend on several factors, including the following:

- successful recruitment of subjects, enrollment in and completion of our ongoing and planned clinical trials;
- initiation and successful recruitment of subjects, enrollment in and completion of additional clinical trials;
- safety, tolerability and efficacy profiles that are satisfactory to the U.S. Food and Drug Administration, or FDA, or any comparable foreign regulatory authority for marketing approval;
- our ability to identify success criteria and endpoints for our clinical trials such that the FDA, the European Medicines Agency, or EMA, and other regulatory authorities will be able to determine the clinical efficacy and safety profile of any product candidates we may develop;
- timely receipt of marketing approvals from applicable regulatory authorities;
- the performance of our future collaborators, if any;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- establishment of supply arrangements with third-party raw materials suppliers and manufacturers;
- establishment of arrangements with third-party manufacturers to obtain finished products that are appropriately packaged for sale;
- developing, validating and maintaining a commercially viable manufacturing process that is compliant with current good manufacturing practices, or cGMPs;
- obtaining and maintaining patent, trade secret protection and regulatory exclusivity, both in the United States and internationally;

- protection of our rights in our intellectual property portfolio;
- successful launch of commercial sales following any marketing approval;
- an acceptable safety profile following any marketing approval;
- commercial acceptance of our products, if approved, by patients, the medical community and third-party payors;
- our ability to compete with other therapies; and
- obtaining and maintaining healthcare coverage and adequate reimbursement.

Many of these factors are beyond our control, including clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any future collaborator. If we are unable to develop, receive marketing approval for and successfully commercialize APL-2 or another product candidate, on our own or with any future collaborator, or experience delays as a result of any of these factors or otherwise, our business could be substantially harmed.

If clinical trials of our product candidates fail to satisfactorily demonstrate safety and efficacy to the FDA and other regulators, we, or any future collaborators, may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.

We, and any future collaborators, are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Foreign regulatory authorities, such as the EMA, impose similar requirements. We have not previously submitted a new drug application, or NDA, to the FDA or similar drug approval filings to comparable foreign regulatory authorities for any of our product candidates. We, and any future collaborators, may never receive such approvals. We, and any future collaborators, must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we will be able to obtain these approvals.

Clinical testing is expensive, is difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. The clinical development of our product candidates is susceptible to the risk of failure inherent at any stage of product development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of adverse events that are severe or medically or commercially unacceptable, failure to comply with protocols or applicable regulatory requirements and determination by the FDA or any comparable foreign regulatory authority that a product candidate may not continue development or is not approvable. It is possible that even if one or more of our product candidates has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials we may fail to detect toxicity of or intolerability caused by our product candidates, or mistakenly believe that our product candidates are toxic or not well tolerated when that is not in fact the case. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we cannot be certain that we will not face additional setbacks. It is possible that any of our development programs may be placed on full or partial clinical hold by regulatory authorities at any point, which would delay and possibly prevent further development of our product candidates.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us, or any future collaborators, and impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. Moreover, if we, or any future collaborators, are required to conduct

additional clinical trials or other testing of our product candidates beyond the trials and testing that we or they contemplate, if we or they are unable to successfully complete clinical trials of our product candidates or other testing or the results of these trials or tests are unfavorable, uncertain or are only modestly favorable, or there are unacceptable safety concerns associated with our product candidates, we, or any future collaborators may:

- incur additional unplanned costs;
- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- be required to remove the product from the market after obtaining marketing approval.

In addition, investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services, including equity awards and option grants, and may have other financial interests in our company. We are required to collect and provide financial disclosure notifications or certifications for our clinical investigators to the FDA. If the FDA concludes that a financial relationship between us and a clinical investigator has created a conflict of interest or otherwise affected interpretation of the trial, the FDA may question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA and may ultimately lead to the denial of marketing approval of our current and future product candidates.

Our failure to successfully complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our product candidates would significantly harm our business.

Adverse events or undesirable side effects caused by, or other unexpected properties of, any of our product candidates may be identified during development that could delay or prevent their marketing approval or limit their use.

Adverse events or undesirable side effects caused by, or other unexpected properties of, our product candidates could cause us, any future collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our product candidates and could result in a more restrictive label, or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. For example, by design APL-2 has immunosuppressive effects and, in some cases, may be administered to patients with underlying significantly compromised health. Administration of our product candidates could make patients more susceptible to infection.

We voluntarily halted a Phase 1 clinical trial of a nebulized formulation of APL-1 in healthy volunteers after two subjects developed signs and symptoms consistent with a bacterial infection that were considered to be serious adverse events and possibly related to the pharmacology of APL-1. APL-2 is a conjugate of APL-1 formulated for subcutaneous and intravitreal administration. We vaccinate subjects against certain bacterial pathogens in all of our ongoing trials involving systemic administration of APL-2. However, there can be no assurance that these efforts will prevent serious adverse effects, including bacterial infection.

In addition, in preclinical studies of APL-2, we observed evidence of minimal to mild kidney toxicity when animals were administered relatively higher doses of APL-2 than the doses we intend to use in the treatment of

patients. We believe this kidney toxicity is likely associated with the presence of polyethylene glycol, or PEG, which is a component of APL-2. If such kidney toxicity, or other adverse effects, were to arise in patients being treated with APL-2 or any other of our product candidates, it could require us to halt, delay or interrupt clinical trials of such product candidate or adversely affect our ability to obtain requisite approvals to advance the development and commercialization of such product candidate.

In our Phase 2 trial of APL-2 in patients with GA, the most frequently reported adverse events were associated with the injection procedure in the study eye. These adverse events included two cases of confirmed endophthalmitis, which is inflammation in the eye typically caused by infection, and one case of presumed endophthalmitis where the culture tested negative for bacterial growth. In addition, during the 12-month treatment period and the subsequent six-month period during which no treatment was administered, we observed a higher incidence of new onset exudation, or fluid leakage in the retinas of eyes in which exudation had not previously been reported, in the study eyes treated with APL-2, predominantly in patients with a history of wet AMD in the non-study eye, or fellow eye. Specifically, we observed that, after the 12-month treatment period and the six-month monitoring period, 21% of patients who received administration of APL-2 every month and 9% of patients who received administration of APL-2 every other month showed new onset exudation in the study eye as compared to 1% of the sham group. As we continue development of APL-2 for GA, if a significant number of patients develop new onset exudation, then we may need to limit development of intravitreal APL-2 to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective.

Serious adverse events have also been reported in our Phase 1b clinical trials of APL-2 for paroxysmal nocturnal hemoglobinuria, or PNH. In our Phase 1b trial of APL-2 in patients receiving treatment with eculizumab, one serious adverse event was noted as possibly related to the administration of APL-2. The patient with this serious adverse event experienced liver pain and elevated liver enzyme levels. As a result, treatment with APL-2 was temporarily discontinued but treatment with eculizumab continued. This discontinuation was followed by a recurrence of anemia and required a blood transfusion, and treatment with APL-2 was reinitiated. Following resumption of treatment, the patient had surgery, which resulted in a lowering of liver enzyme levels. In late October 2017, in our Phase 1b trial of APL-2 in treatment-naïve patients, we learned that one patient with concomitant aplastic anemia developed bone marrow failure after one year of treatment with APL-2. Treatment with APL-2 was discontinued on November 14, 2017. The investigator determined that the bone marrow failure in this patient was not related to the administration of APL-2. Development of bone marrow failure is a known risk in patients with PNH. In third-party studies, bone marrow failure occurred in between 15% and 30% of PNH patients, regardless of treatment with eculizumab. However, there can be no assurance that the administration of APL-2 could not have contributed to the bone marrow failure experienced by this patient.

If any of our product candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, we, or any future collaborators, may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause undesirable or unexpected side effects that prevented further development of the compound.

In addition, clinical trials by their nature utilize a sample of the potential patient population. However, with a limited number of subjects and limited duration of exposure, rare and severe side effects of our product candidates may only be uncovered when a significantly larger number of patients are exposed to the product. If safety problems occur or are identified after one of our products reaches the market, the FDA or comparable non-U.S. regulatory authorities may require that we amend the labeling of our product, recall our product, or even withdraw approval for our product.

If we, or any future collaborators, experience any of a number of possible unforeseen events in connection with clinical trials of our product candidates, potential clinical development, marketing approval or commercialization of our product candidates could be delayed or prevented.

We, or any future collaborators, may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent clinical development, marketing approval or commercialization of our product candidates, including:

- clinical trials of our product candidates may produce unfavorable or inconclusive results;
- we, or any future collaborators, may decide, or regulators may require us or them, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we, or any future collaborators, anticipate, patient enrollment in these clinical trials may be slower than we, or any future collaborators, anticipate or participants may drop out of these clinical trials at a higher rate than we, or any future collaborators, anticipate;
- the cost of planned clinical trials of our product candidates may be greater than we anticipate;
- our third-party contractors or those of any future collaborators, including those manufacturing our product candidates or components or ingredients thereof or conducting clinical trials on our behalf or on behalf of any future collaborators, may deviate from the trial protocol, fail to comply with regulatory requirements or fail to meet their contractual obligations to us or any future collaborators in a timely manner or at all;
- regulators or institutional review boards may not authorize us, any future collaborators or our or their investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we, or any future collaborators, may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- patients that enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial's duration;
- we, or any future collaborators, may have to delay, suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate, such as occurred in our Phase 1 clinical trial of APL-1;
- regulators or institutional review boards may require that we, or any future collaborators, or our or their investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate or findings of undesirable effects caused by a chemically or mechanistically similar product or product candidate;
- the FDA or comparable foreign regulatory authorities may disagree with our, or any future collaborators', clinical trial designs or our or their interpretation of data from preclinical studies and clinical trials;
- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third-party manufacturers with which we, or any future collaborators, enter into agreements for clinical and commercial supplies;
- the supply or quality of raw materials or manufactured product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient to obtain marketing approval.

Product development costs for us, or any future collaborators, will increase if we, or they, experience delays in testing or pursuing marketing approvals and we, or they, may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization of our product candidates. We do not know whether any preclinical tests or clinical trials will begin as planned, will need to be restructured, or will be completed on schedule or at all. Significant preclinical study or clinical trial delays also could shorten any periods during which we, or any future collaborators, may have the exclusive right to commercialize our product candidates or allow our competitors, or the competitors of any future collaborators, to bring products to market before we, or any future collaborators, do and impair our ability, or the ability of any future collaborators, to successfully commercialize our product candidates and may harm our business and results of operations. In addition, many of the factors that lead to clinical trial delays may ultimately lead to the denial of marketing approval of any of our product candidates.

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

We, or any future collaborators, may not be able to initiate or continue clinical trials for any of our product candidates if we, or they, are unable to locate and enroll a sufficient number of eligible patients to participate in clinical trials as required by the FDA or comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the proximity of patients to clinical sites;
- the patient referral practices of physicians;
- the eligibility criteria for the trial;
- the design of the clinical trial;
- efforts to facilitate timely enrollment;
- competing clinical trials; and
- clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

In particular, the successful completion of our clinical development program for APL-2 for the treatment of PNH is dependent upon our ability to enroll a sufficient number of patients with PNH. PNH is a rare disease with a small patient population, and many of those patients are treated with eculizumab, marketed as Soliris by Alexion Pharmaceuticals, Inc., or Alexion. Further, there are only a limited number of specialist physicians that regularly treat patients with PNH and major clinical centers that support PNH treatment are concentrated in a few geographic regions. In addition, other companies are conducting clinical trials and have announced plans for future clinical trials that are seeking, or are likely to seek, to enroll patients with PNH and patients are generally only able to enroll in a single trial at a time. Both patients and their physicians may be reluctant to forgo, discontinue or otherwise alter existing, approved life-saving therapeutic approaches. Given the severe and life-threatening nature of PNH and the expectation that many patients will be on treatment with eculizumab, we may encounter difficulty in recruiting a sufficient number of patients for our trials. The small population of patients, competition for these patients, the nature of the disease and limited trial sites may make it difficult for us to enroll enough patients to complete our clinical trials of APL-2 in PNH in a timely and cost-effective manner.

Our inability, or the inability of any future collaborators, to enroll a sufficient number of patients for our, or their, clinical trials could result in significant delays or may require us or them to abandon one or more clinical

trials altogether. Enrollment delays in our, or their, clinical trials may result in increased development costs for our product candidates, delay or halt the development of and approval processes for our product candidates and jeopardize our, or any future collaborators', ability to commence sales of and generate revenues from our product candidates, which could cause the value of our company to decline and limit our ability to obtain additional financing, if needed.

Results of preclinical studies and Phase 1 and Phase 2 clinical trials may not be predictive of results of later clinical trials.

The outcome of preclinical studies and Phase 1 and Phase 2 clinical trials may not be predictive of the success of later clinical trials, and preliminary or interim results of clinical trials do not necessarily predict final results. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier stages of clinical development, and we could face similar setbacks. Similarly, the design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced.

We have limited experience in designing pivotal clinical trials and may be unable to design and execute a clinical trial to support marketing approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we, or any future collaborators, believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates.

Some of the data we present on the use of APL-2 for the treatment of GA is drawn from *post hoc* analyses of data subsets from our Phase 2 clinical trial. While we believe these data may be useful in informing the design of future Phase 3 clinical trials for APL-2, *post hoc* analyses performed after unmasking trial results can result in the introduction of bias and may not be predictive of success in Phase 3 clinical trials.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. For instance, the Phase 3 clinical trials in GA will be similar in design to the Phase 2 clinical trial, except that patients will be treated with APL-2 for 24 months rather than 12 months and there will not be a six-month monitoring period following treatment. Additionally, unlike the Phase 2 trial, GA lesion size will be measured by total area rather than mean change in the square root of GA lesion size. We also expect that we will set statistical significance at a p-value of 0.05 or less, meaning that there is a 1-in-20 or less probability that the observed results occurred by chance rather than as a treatment effect. In our Phase 2 trial in GA, we set statistical significance as a p-value of 0.1 or less, meaning that there is a 1-in-10 or less probability that the observed results occurred by chance. If we fail to receive positive results in clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced product candidates, and, correspondingly, our business and financial prospects would be negatively impacted.

If we fail to develop and commercialize other product candidates, we may be unable to grow our business.

Although the development and commercialization of APL-2 is our primary focus, as part of our growth strategy, we are developing a pipeline of product candidates for the treatment of complement-dependent diseases. These other product candidates will require additional, time-consuming and costly development efforts prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA and/or applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical

product development, including the possibility that the product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, there can be no assurance that any such products that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective than other commercially available alternatives.

We have never obtained marketing approval for a product candidate and we may be unable to obtain, or may be delayed in obtaining, marketing approval for any of our product candidates.

We have never obtained marketing approval for a product candidate. It is possible that the FDA may refuse to accept for substantive review any NDAs that we submit for our product candidates or may conclude after review of our data that our application is insufficient to obtain marketing approval of our product candidates. If the FDA does not accept or approve our NDAs for any of our product candidates, including APL-2, it may require that we conduct additional clinical trials, preclinical studies or manufacturing validation studies and submit that data before it will reconsider our applications. Depending on the extent of these or any other FDA-required trials or studies, approval of any NDA or application that we submit may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional trials or studies, if performed and completed, may not be considered sufficient by the FDA to approve our NDAs.

Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing our product candidates, generating revenues and achieving and sustaining profitability. If any of these outcomes occur, we may be forced to abandon our development efforts for our product candidates, which could significantly harm our business.

Even if any of our product candidates receives marketing approval, we or others may later discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, which could compromise our ability, or that of any future collaborators, to market the product.

Clinical trials of our product candidates are conducted in carefully defined sets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials, or those of any future collaborator, may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, we, or others, discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we, or any future collaborators, may be required to recall the product, change the way the product is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular product;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we, or any future collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or any future collaborators, could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of these events could harm our business and operations, and could negatively impact our stock price.

Even if one of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, in which case we may not generate significant revenues or become profitable.

We have never commercialized a product, and even if one of our product candidates is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies. Eculizumab is the only drug approved for the treatment of PNH, and even if we are able to obtain marketing approval of APL-2 for the treatment of PNH, we may not be able to successfully convince physicians or patients to switch from eculizumab to APL-2. This may be particularly true with respect to eculizumab as many in the medical community believe that patients with PNH on eculizumab may experience sudden and excessive blood cell lysis, or rupture, leading to anemia, blood clots and other medical problems, when they stop receiving eculizumab. In addition, even if we are able to demonstrate our product candidates' safety and efficacy to the FDA and other regulators, safety concerns in the medical community may hinder market acceptance.

Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If any of our product candidates is approved but does not achieve an adequate level of market acceptance, we may not generate significant revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the product;
- the potential advantages of the product compared to competitive therapies;
- the prevalence and severity of any side effects;
- the clinical indications for which the product is approved;
- whether the product is designated under physician treatment guidelines as a first-, second- or third-line therapy;
- our ability, or the ability of any future collaborators, to offer the product for sale at competitive prices;
- the product's convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;
- limitations or warnings, including distribution or use restrictions contained in the product's approved labeling;
- the strength of sales, marketing and distribution support;
- the approval of other new products for the same indications;
- the timing of market introduction of our approved products as well as competitive products;
- adverse publicity about the product or favorable publicity about competitive products;
- potential product liability claims;
- changes in the standard of care for the targeted indications for the product; and
- availability and amount of coverage and reimbursement from government payors, managed care plans and other third-party payors.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we intend to focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of both their potential for marketing approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the product candidate.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution arrangements with third parties, we may not be successful in commercializing any product candidates if approved.

We do not have a sales, marketing or distribution infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties.

We plan to build focused capabilities to commercialize development programs for certain indications where we believe that the medical specialists for the indications are sufficiently concentrated to allow us to effectively promote the product with a targeted sales team. The development of sales, marketing and distribution capabilities will require substantial resources, will be time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we could have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and our investment could be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire or retain a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets that we plan to target. If we are unable to establish or retain a sales force and marketing and distribution capabilities, our operating results may be adversely affected. If a potential partner has development or commercialization expertise that we believe is particularly relevant to one of our products, then we may seek to collaborate with that potential partner even if we believe we could otherwise develop and commercialize the product independently.

In certain indications, we may seek to enter into collaborations that we believe may contribute to our ability to advance development and ultimately commercialize our product candidates. We may also seek to enter into collaborations where we believe that realizing the full commercial value of our development programs will require access to broader geographic markets or the pursuit of broader patient populations or indications. As a result of entering into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues may be lower, perhaps substantially lower, than if we were to directly market and sell products in those markets. Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to us. In addition, we may have little or no control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively.

If we do not establish sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing any of our product candidates that receive marketing approval.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new products is highly competitive. We expect that we, and any future collaborators, will face significant competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to any of our product candidates that we, or any future collaborators, may seek to develop or commercialize in the future, including from therapies that act through the complement system and therapies that use different approaches.

There are currently no approved treatments for GA. We are aware that there are a number of companies that are actively developing product candidates for the treatment of GA, including the following product candidates that are in clinical development: CLG561, an anti-properdin monoclonal antibody being developed as a monotherapy or adjunctive therapy with LFG316, an anti-C5 monoclonal antibody being developed by Novartis AG that is in Phase 2 clinical trials; Zimura, a C5 inhibitor being developed by Ophthotech Corporation that is in Phase 2/3 clinical trials; and other product candidates that do not target the complement system that are in Phase 2 clinical trials, including compounds being developed by Allergan PLC and Regenerative Patch Technologies. In September and November 2017, F. Hoffmann-La Roche, or Roche, announced that lampalizumab, a complement factor D inhibitor being developed by Roche for the treatment of GA, had failed to meet its primary endpoint in its Phase 3 clinical trials.

The principal competitor for PNH, and possibly other indications in our hematology and nephrology programs, is eculizumab, a C5 inhibitor, which is marketed as Soliris by Alexion and is the only drug approved for the treatment of PNH. Alexion is conducting Phase 3 trials of ALXN1210 for patients with PNH. ALXN1210 is designed to have a longer half-life and greater inhibition of C5 than eculizumab. We are aware of a number of other companies that are actively developing product candidates for the treatment of PNH, including a product candidate directed at C3 complement inhibition that is currently in Phase 1 clinical development by Amyndas Pharmaceuticals SA; product candidates directed at C5 complement inhibition such as ALN-CC5, an RNAi therapeutic targeting C5 being developed by Alnylam Pharmaceuticals, Inc. that is in early clinical trials; Coversin, a small protein inhibitor of C5 being developed by Akari Therapeutics, Plc. that is in Phase 2 clinical trials; Ra101495, a cyclic peptide inhibitor of C5 that is currently in Phase 2 trials by Ra Pharmaceuticals, Inc., and LFG316, an anti-C5 monoclonal antibody that is currently in Phase 2 trials by Novartis; and other product candidates directed at other mechanisms of complement inhibition such as NM-9405, an anti-properdin antibody in preclinical development by NovelMed Therapeutics, Inc., and ACH-4471 (previously ACH-CFDIS), an orally available small molecule inhibitor of complement factor D, that is currently in early clinical development by Achillion Pharmaceuticals, Inc. Amgen is developing ABP959, a biosimilar for eculizumab that is in early clinical development. The approval of a biosimilar or a generic to one of our products or a product with which we compete could have a material impact on our business because it may be significantly less costly to bring to market and may be priced significantly lower than our products or the other products with which we compete.

There are no currently marketed drug treatments for autoimmune hemolytic anemia, or AIHA, but there are currently treatments in development for AIHA, including: fostamatinib, a spleen tyrosine kinase inhibitor being developed by Rigel Pharmaceuticals, Inc., which is in Phase 2 trials, and TNT-009/BIVV009, a C1s monoclonal antibody inhibitor, which is being developed by Bioverativ Inc., and is in early clinical trials in patients with cold agglutinin disease, a subtype of AIHA. There are no currently marketed drug treatments for complement-dependent nephropathies, but OMS721, a human monoclonal antibody to mannose-binding lectin-associated serine protease-2 (MASP-2) that blocks the lectin pathway, is being developed by Omeros Corp. as a treatment for IgA nephropathy and is entering Phase 3 clinical trials.

Our competitors may succeed in developing, acquiring or licensing technologies and products that are more effective, have fewer side effects or more tolerable side effects or are less costly than any product candidates that we are currently developing or that we may develop, which could render our product candidates obsolete and noncompetitive.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we, or any future collaborators, may develop. Our competitors also may obtain FDA or other marketing approval for their products before we, or any future collaborators, are able to obtain approval for ours, which could result in our competitors establishing a strong market position before we, or any future collaborators, are able to enter the market.

Many of our existing and potential future competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining marketing approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, the development of our product candidates.

If the FDA or comparable foreign regulatory authorities approve generic versions of any of our products that receive marketing approval, or such authorities do not grant our products appropriate periods of data exclusivity before approving generic versions of our products, the sales of our products could be adversely affected.

Once an NDA is approved, the product covered thereby becomes a “reference-listed drug” in the FDA’s publication, “Approved Drug Products with Therapeutic Equivalence Evaluations,” or the Orange Book. Manufacturers may seek approval of generic versions of reference-listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical trials. Rather, the applicant generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference-listed drug and that the generic version is bioequivalent to the reference-listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference-listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference-listed drug may be typically lost to the generic product.

The FDA may not approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference-listed drug has expired. The Federal Food, Drug, and Cosmetic Act, or FDCA, provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity, or NCE. Specifically, in cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference-listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the reference-listed drug. It is unclear whether the FDA will treat the active ingredients in our product candidates as NCEs and, therefore, afford them five years of NCE data exclusivity if they are approved. If any product we develop does not receive five years of NCE exclusivity, the FDA may approve generic versions of such product three years after its date of approval, subject to the requirement that the ANDA applicant certifies to any patents listed for our products in the Orange Book. Manufacturers may seek to launch these generic products following the expiration of the applicable marketing exclusivity period, even if we still have patent protection for our product.

Competition that our products may face from generic versions of our products could negatively impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on our investments in those product candidates.

Even if we, or any future collaborators, are able to commercialize any product candidate that we, or they, develop, the product may become subject to unfavorable pricing regulations, third-party payor reimbursement practices or healthcare reform initiatives, any of which could harm our business.

The commercial success of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by third-party payors, including government health administration authorities and private health coverage insurers. If coverage and reimbursement is not available, or reimbursement is available only to limited levels, we, or any future collaborators, may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or any future collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or their investments. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we, or any future collaborators, might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability or the ability of any future collaborators to recoup our or their investment in one or more product candidates, even if our product candidates obtain marketing approval.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability, and the ability of any future collaborators, to commercialize any of our product candidates will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from third-party payors. Third-party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and abroad. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability or that of any future collaborators to sell our product candidates profitably. These payors may not view our products, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or those of any future collaborators, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us, or any future collaborators, to decrease the price we, or they, might establish for products, which could result in lower than anticipated product revenues. If the prices for our products, if any, decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer.

The commercial potential of our products depends in part on reimbursement by government health administration authorities, private health insurers and other organizations. If we are unable to obtain coverage or reimbursement for our products, as monotherapy or in combination with other therapies, including possible combinations with eculizumab, at the levels anticipated, our financial condition could be harmed. Additionally, if new compounds currently in development by potential competitors, including biosimilars of eculizumab, obtain marketing approval, there may be downward pressure on reimbursement levels for therapies in our target disease areas, which could have a negative impact on our ability to achieve and maintain profitability.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the product and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

In addition, increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. We cannot be sure that coverage will be available for any product candidate that we, or any future collaborator, commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any of our product candidates for which we, or any future collaborator, obtain marketing approval could significantly harm our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Product liability lawsuits against us could divert our resources, cause us to incur substantial liabilities and limit commercialization of any products that we may develop.

We face an inherent risk of product liability claims as a result of the clinical testing of our product candidates despite obtaining appropriate informed consents from our clinical trial participants. We will face an even greater risk if we or any future collaborators commercially sell any product that we may or they may develop. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend resulting litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

Although we maintain product liability insurance coverage in the amount of up to $20.0 million in the aggregate and clinical trial liability insurance of up to $20.0 million in the aggregate, this insurance may not fully cover potential liabilities that we may incur. The cost of any litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage if we commercialize any product that receives marketing approval. In addition, insurance coverage is becoming increasingly expensive. If we are unable to maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could harm our business, financial condition, results of operations and prospects.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct our clinical trials. If they do not perform satisfactorily, our business could be harmed.

We do not independently conduct clinical trials of our product candidates. We rely, and expect to continue to rely, on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials of APL-2 and any other product candidate that we develop. Any of these third parties may terminate their engagements with us under certain circumstances. We may not be able to enter into alternative arrangements or do so on commercially reasonable terms. In addition, there is a natural transition period when a new contract research organization begins work. As a result, delays would likely occur, which could negatively impact our ability to meet our expected clinical development timelines and harm our business, financial condition and prospects.

Further, although our reliance on these third parties for clinical development activities limits our control over these activities, we remain responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards. For example, notwithstanding the obligations of a contract research organization for a trial of one of our product candidates, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as current Good Clinical Practices, or cGCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The FDA enforces these cGCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and institutional review boards. If we or our third-party contractors fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our product candidates, which would delay the marketing approval process. We cannot be certain that, upon inspection, the FDA will determine that any of our clinical trials comply with cGCPs. Similar regulatory requirements apply outside the United States, including the International Council for Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use, or ICH. We are also required to register clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, the third parties conducting clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time, skill and resources to our ongoing development programs. These contractors may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates. If that occurs, we will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. In such an event, our financial results and the commercial prospects for any product candidates that we seek to develop could be harmed, our costs could increase and our ability to generate revenues could be delayed, impaired or foreclosed.

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

We currently have no manufacturing facilities, and a relatively small number of personnel with manufacturing experience who can oversee the manufacturing process. We rely on contract manufacturers to

manufacture, store and distribute both drug substance and drug product required for our clinical trials. We plan to continue to rely upon contract manufacturers, and, potentially collaboration partners, to manufacture commercial quantities of our products, if approved. We may be unable to establish any agreements with contract manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with contract manufacturers, reliance on contract manufacturers entails additional risks, including:

- manufacturing delays if our third-party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them, or if unforeseen events in the manufacturing process arise;
- the possible termination or nonrenewal of agreements by our third-party contractors at a time that is costly or inconvenient for us;
- the possible breach by the third-party contractors of our agreements with them;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the possible mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;
- the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

We currently rely, and expect to continue to rely, on a small number of third-party contract manufacturers to supply most of our supply of active pharmaceutical ingredients and required finished product for our preclinical studies and clinical trials. We do not have long-term supply agreements with any of these third parties. If any of our existing manufacturers should become unavailable to us for any reason, we may incur delays in identifying or qualifying replacements. We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our contract manufacturers or distributors could delay clinical development or marketing approval of our product candidates or commercialization of any resulting products, producing additional losses and depriving us of potential product revenue. For example, in the past we have experienced issues associated with the manufacturing process for APL-2 that have resulted in delays in the supply of APL-2. These delays resulted in us incurring additional costs and delays in our PNH development program. If we experience other issues or delays in the future, our development of APL-2 may be materially delayed and our business adversely affected.

Any manufacturing problem, the loss of a contract manufacturer or any loss of storage could be disruptive to our operations, delay our clinical trials and, if our products are approved for sale, result in lost sales. Additionally, we rely on third parties to supply the raw materials needed to manufacture our product candidates. For example, one company currently produces most of the PEG that is used in pharmaceutical and drug development globally. PEG is a component of APL-2. If this supplier of PEG experiences manufacturing and supply problems with respect to PEG, then the manufacturers with whom we contract may have difficulty in procuring PEG for the supply and manufacture of APL-2. Any reliance on suppliers may involve several risks, including a potential inability to obtain critical materials and reduced control over production costs, delivery schedules, reliability and quality. Any unanticipated disruption to our contract manufacturing caused by problems at suppliers could delay shipment of our product candidates, increase our cost of goods sold and result in lost sales with respect to any approved products.

If any of our product candidates are approved by any regulatory agency, we will need to enter into agreements with third-party contract manufacturers for the commercial production and distribution of those products. It may be difficult for us to reach agreement with a contract manufacturer on satisfactory terms or in a timely manner. In addition, we may face competition for access to manufacturing facilities as there are a limited

number of contract manufacturers operating under cGMPs that can manufacture our product candidates. Consequently, we may not be able to reach agreement with third-party manufacturers on satisfactory terms, which could delay our commercialization efforts.

Third-party manufacturers are required to comply with cGMPs and similar regulatory requirements outside the United States, such as the ICH. Facilities used by our third-party manufacturers must be approved by the FDA after we submit an NDA and before potential approval of the product candidate. Similar regulations apply to manufacturers of our product candidates for use or sale in foreign countries. We do not control the manufacturing process and are completely dependent on our third-party manufacturers for compliance with the applicable regulatory requirements for the manufacture of our product candidates. If our manufacturers cannot successfully manufacture material that conforms to our specifications or the strict regulatory requirements of the FDA and any applicable foreign regulatory authority, they will not be able to secure the applicable approval for their manufacturing facilities. If these facilities are not approved for commercial manufacture, we may need to find alternative manufacturing facilities, which could result in delays in obtaining approval for the applicable product candidate.

In addition, our manufacturers are subject to ongoing periodic inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements both prior to and following the receipt of marketing approval for any of our product candidates. Some of these inspections may be unannounced. Failure by any of our manufacturers to comply with applicable cGMPs or other regulatory requirements could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspensions or withdrawals of approvals, operating restrictions, interruptions in supply and criminal prosecutions, any of which could significantly impact the available supplies of our product candidates and harm our business, financial condition and results of operations.

We are developing a custom, on-body drug delivery system that would enable patients to self-administer APL-2 through subcutaneous infusion. While this device is in development, we will use one or more commercially available ambulatory infusion pumps in our ongoing and planned clinical trials. The development of a custom drug delivery system may be delayed or we may not be successful in developing a custom drug delivery system and may need to continue to rely on commercially available ambulatory infusion pumps. Any reliance on third-party infusion pumps may involve several risks, including reduced control over costs, delivery schedules, reliability and quality.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may harm our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

We may seek to establish collaborations and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

We may seek to establish one or more collaborators for the development and commercialization of one or more of our product candidates. Likely collaborators may include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. In addition, if we are able to obtain marketing approval for product candidates from foreign regulatory authorities, we intend to enter into strategic relationships with international biotechnology or pharmaceutical companies for the commercialization of such product candidates outside of the United States.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator’s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator’s evaluation of a number of factors. Those factors may include the potential differentiation of our product candidates from competing product candidates, design or results of clinical trials, the likelihood of approval by

the FDA or comparable foreign regulatory authorities and the regulatory pathway for any such approval, the potential market for the product candidate, the costs and complexities of manufacturing and delivering the product to patients and the potential of competing products. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available for collaboration and whether such a collaboration could be more attractive than the one with us for our product candidate. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

Collaborations are complex and time-consuming to negotiate and document. Further, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

Any collaboration agreements that we enter into in the future may contain restrictions on our ability to enter into potential collaborations or to otherwise develop specified product candidates. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense.

If we enter into collaborations with third parties for the development and commercialization of our product candidates, our prospects with respect to those product candidates will depend in significant part on the success of those collaborations.

We may seek to enter into collaborations for the development and commercialization of certain of our product candidates. We have not entered into any collaborations to date. If we enter into such collaborations, we will have limited control over the amount and timing of resources that our collaborators will dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on any future collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, any future collaborators may have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms.

Collaborations involving our product candidates pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs, based on clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;

- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between the collaborators and us regarding ownership of or other rights in the intellectual property generated in the course of the collaborations; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If any future collaborator of ours is involved in a business combination, it could decide to delay, diminish or terminate the development or commercialization of any product candidate licensed to it by us.

Risks Related to Our Intellectual Property

If we fail to comply with our obligations under our existing and any future intellectual property licenses with third parties, we could lose license rights that are important to our business.

We are a party to patent license agreements with Penn under which we license patent rights relating to a family of compounds for use in all fields. The licensed patent rights include issued U.S. and foreign patents with claims that recite a class of compounds generically covering our lead product candidate, APL-2, and that specifically recite APL-1. We may enter into additional license agreements in the future. Our license agreements with Penn impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations under these licenses, our licensors may have the right to terminate these license agreements, in which event we might not be able to market any product that is covered by these agreements, or our licensors may convert the license to a non-exclusive license, which could negatively impact the value of the product candidate being developed under the license agreement. Termination of these license agreements or reduction or elimination of our licensed rights may also result in our having to negotiate new or reinstated licenses with less favorable terms.

If we are unable to obtain and maintain sufficient patent protection for our product candidates, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our product candidates may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary product candidates. If we do not adequately protect our intellectual property rights, competitors may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. To protect our proprietary position, we file patent applications in the United States and abroad related to our novel product candidates that are important to our business; we also license or purchase patent applications filed by others. The patent application and approval process is expensive and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner.

Agreements through which we license patent rights may not give us control over patent prosecution or maintenance, so that we may not be able to control which claims or arguments are presented and may not be able to secure, maintain, or successfully enforce necessary or desirable patent protection from those patent rights. We have not had and do not have primary control over patent prosecution and maintenance for certain of the patents and patent applications we license, and therefore cannot guarantee that these patents and applications will be prosecuted in a manner consistent with the best interests of our business. We cannot be certain that patent prosecution and maintenance activities by our licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents.

We, or any future partners, collaborators, or licensees, may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to strengthen our patent position. Moreover, in some circumstances, we might not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering any technology that we may license from third parties in the future. These patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Our license agreements with Penn provide that Penn has the right under certain circumstances to control the preparation, prosecution and maintenance of the underlying patent rights.

It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope, or patent term adjustments. If we or our partners, collaborators, licensees, or licensors, whether current or future, fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our partners, collaborators, licensees, or licensors are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of our patents or patent applications, such patents may be invalid and/or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. In addition, the determination of patent rights with respect to pharmaceutical compounds commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain.

Pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Similarly, we cannot be certain that parties from whom we do or may license or purchase patent rights were the first to make relevant claimed inventions, or were the first to file for patent protection for them. If third parties have filed patent applications on inventions claimed in our patents or applications on or before March 15, 2013, an interference proceeding in the United States can be initiated by such third parties to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. If third parties have filed such applications after March 15, 2013, a derivation proceeding in the United States can be initiated by such third parties to determine whether our invention was derived from theirs.

Moreover, because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, our patents or pending patent applications may be challenged in the courts or patent offices in the United States and abroad. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found. If such prior art exists, it may be used to invalidate a patent, or may prevent a patent from issuing from a pending patent application. For example, such patent filings may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or to other patent offices around the world. Alternately or additionally, we may become involved in post-grant review procedures, oppositions, derivations, proceedings, reexaminations, inter partes review or interference proceedings, in the United States or elsewhere, challenging patents or patent applications in which we have rights, including patents on which we rely to protect our business. An adverse determination in any such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Furthermore, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. As a result, the inventorship or ownership of our intellectual property may be challenged in the future.

Pending and future patent applications may not result in patents being issued which protect our business, in whole or in part, or which effectively prevent others from commercializing competitive products. Our issued patents or any patents that may issue in the future may be invalidated or interpreted narrowly, such that they fail to provide us with any significant competitive advantage. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the United States. For example, patent laws in various jurisdictions, including significant commercial markets such as Europe, restrict the patentability of methods of treatment of the human body more than United States law does.

Issued patents that we have or may obtain or license may not provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may also seek approval to market their own products similar to or otherwise competitive with our products. Alternatively, our competitors may seek to market generic versions of any approved products by submitting ANDAs to the FDA in which they claim that patents owned or licensed by us are invalid, unenforceable or not infringed. In these circumstances, we may need to defend or assert our patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid or unenforceable, or find that our competitors are competing in a non-infringing manner. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

Pursuant to the terms of some of our license agreements with third parties, some of our third-party licensors have the right, but not the obligation in certain circumstances to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents. Even if we are permitted to pursue such enforcement or defense, we will require the cooperation of our licensors, and cannot guarantee that we would receive it and on what terms. We cannot be certain that our licensors will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. If we cannot obtain patent protection, or enforce existing or future patents against third parties, our competitive position and our financial condition could suffer.

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be negatively impacted and our business would be harmed.

In addition to the protection afforded by patents, we also rely on trade secret protection for certain aspects of our intellectual property. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, consultants, independent contractors, advisors, contract manufacturers, suppliers and other third parties. We also enter into confidentiality and invention or patent assignment agreements with employees and certain consultants. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. Further, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our business and competitive position could be harmed.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. An adverse outcome in a litigation or proceeding involving one or more of our patents could limit our ability to assert those patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could adversely affect the price of shares of our common stock. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our product candidates without infringing the intellectual property and other proprietary rights of third parties. Third parties may have U.S. and non-U.S. issued patents and pending patent applications relating to compounds and methods of use for the treatment of the disease indications for which we are developing our product candidates or relating to the use of complement inhibition that may cover our product candidates or approach to complement inhibition. For example, we are aware of a U.S. patent with claims that could be construed to cover APL-2. Although we believe that these claims, if construed to cover APL-2, would be invalid due to various prior art disclosures available more than a year before the priority date of the U.S. patent, there are no assurances that a court would agree. If any third-party patents or patent applications are found to cover our product candidates or their methods of use or our approach to complement inhibition, we may not be free to manufacture or market our product candidates as planned without obtaining a license, which may not be available on commercially reasonable terms, or at all.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our products candidates, including interference proceedings before the USPTO. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may be accused of infringing. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Accordingly, third parties may assert infringement claims against us based on existing or future intellectual property rights. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

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

Some of our intellectual property that was discovered through government-funded programs may be subject to federal regulation such as "march-in" rights, certain reporting requirements, and a preference for U.S.

industry. Compliance with such regulations may limit our exclusive rights, subject us to expenditure of resources with respect to reporting requirements and limit our ability to contract with foreign manufacturers.

Some of our in-licensed intellectual property with respect to our product candidates has been funded in part by the U.S. government and, therefore, would be subject to certain federal regulations pursuant to the Bayh-Dole Act of 1980, or the Bayh-Dole Act. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act. For example, under the "march-in" provisions of the Bayh-Dole Act, the U.S. government may have the right under limited circumstances to require the patent owners to grant exclusive, partially exclusive or non-exclusive rights to third parties for intellectual property discovered through the government-funded program. The U.S. government can exercise its march-in rights if it determines that action is necessary because the patent owner fails to achieve practical application of the new invention or because action is necessary to alleviate health concerns or address the safety needs of the public. Intellectual property discovered under the government-funded program is also subject to certain reporting requirements, compliance with which may require us or our licensors to expend substantial resources. Such intellectual property is also subject to a preference for U.S. industry, which may limit our ability to contract with foreign product manufacturers for products covered by such intellectual property. Intellectual property under such discoveries would be subject to the applicable provisions of the Bayh-Dole Act. Similarly, intellectual property that we license in the future may have been made using government funding and may be subject to the provisions of the Bayh-Dole Act.

Changes to the patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Recent patent reform legislation in the United States, including the Leahy-Smith America Invents Act, or the America Invents Act, could increase those uncertainties and costs. The America Invents Act was signed into law on September 16, 2011, and many of the substantive changes became effective on March 16, 2013. The America Invents Act reformed United States patent law in part by changing the U.S. patent system from a "first to invent" system to a "first inventor to file" system, expanding the definition of prior art, and developing a post-grant review system. This legislation changes United States patent law in a way that may weaken our ability to obtain patent protection in the United States for those applications filed after March 16, 2013.

Further, the America Invents Act created new procedures to challenge the validity of issued patents in the United States, including post-grant review and inter partes review proceedings, which some third parties have been using to cause the cancellation of selected or all claims of issued patents of competitors. For a patent with an effective filing date of March 16, 2013 or later, a petition for post-grant review can be filed by a third party in a nine-month window from issuance of the patent. A petition for inter partes review can be filed immediately following the issuance of a patent if the patent has an effective filing date prior to March 16, 2013. A petition for inter partes review can be filed after the nine-month period for filing a post-grant review petition has expired for a patent with an effective filing date of March 16, 2013 or later. Post-grant review proceedings can be brought on any ground of invalidity, whereas inter partes review proceedings can only raise an invalidity challenge based on published prior art and patents. These adversarial actions at the USPTO review patent claims without the presumption of validity afforded to U.S. patents in lawsuits in U.S. federal courts, and use a lower burden of proof than used in litigation in U.S. federal courts. Therefore, it is generally considered easier for a competitor or third party to have a U.S. patent invalidated in a USPTO post-grant review or inter partes review proceeding than invalidated in a litigation in a U.S. federal court. If any of our patents are challenged by a third party in such a USPTO proceeding, there is no guarantee that we or our licensors or collaborators will be successful in defending the patent, which would result in a loss of the challenged patent right to us.

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations.

Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to enforce our patents. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

We may not be able to enforce our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States are less extensive than those in the United States. The requirements for patentability may differ in certain countries, particularly in developing countries; thus, even in countries where we do pursue patent protection, there can be no assurance that any patents will issue with claims that cover our products. Competitors may use our technologies in jurisdictions where we have not pursued and obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we may obtain patent protection, but where patent enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued or licensed patents and any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, laws of some countries outside of the United States and Europe do not afford intellectual property protection to the same extent as the laws of the United States and Europe. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, including India, China and other developing countries, do not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the United States and Europe. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop and market their own products and, further, may export otherwise infringing products to territories where we have patent protection, if our ability to enforce our patents to stop infringing activities is inadequate. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Agreements through which we license patent rights may not give us sufficient rights to permit us to pursue enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents (or control of enforcement or defense) of such patent rights in all relevant jurisdictions as requirements may vary.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Moreover, such proceedings could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Furthermore, while we intend to protect our intellectual property rights in major markets for our products, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, or Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term extension of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond 14 years from the date of product approval, only one patent may be extended and the extension only applies to those claims covering the approved drug, a method for using it, or a method for manufacturing it. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations and prospects could be materially harmed.

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

Many of our employees and our licensors' employees, including our senior management, were previously employed at universities or at other biotechnology or pharmaceutical companies, including some which may be competitors or potential competitors. Some of these employees, including each member of our senior management, executed proprietary rights, non-disclosure, non-competition and non-solicitation agreements, or similar agreements, in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such third party. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and applications are required to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and applications. The USPTO and various

non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and after a patent has issued. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, the failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our product candidates, our competitive position would be adversely affected.

If we are unable to obtain licenses from third parties on commercially reasonable terms or fail to comply with our obligations under such agreements, our business could be harmed.

It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties. If we are unable to license such technology, or if we are forced to license such technology on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation. Even if we are able to obtain a license, it may be non-exclusive, which could enable our competitors to obtain access to the same technologies licensed to us.

If we fail to comply with our obligations under license agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market, or may be forced to cease developing, manufacturing or marketing, any product that is covered by these agreements or may face other penalties under such agreements. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, cause us to lose our rights under these agreements, including our rights to important intellectual property or technology, or impede, delay or prohibit the further development or commercialization of one or more product candidates that rely on such agreements.

Risks Related to Regulatory Approval and Marketing of Our Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the regulatory approval process is expensive, time consuming and uncertain and may prevent us or any future collaborators from obtaining approvals for the commercialization of some or all of our product candidates. As a result, we cannot predict when or if, and in which territories, we, or any future collaborators, will obtain marketing approval to commercialize a product candidate.

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of products are subject to extensive regulation by the FDA and comparable foreign regulatory authorities. We, and any future collaborators, are not permitted to market our product candidates in the United States or in other countries until we, or they, receive approval of an NDA from the FDA or marketing approval from applicable regulatory authorities outside the United States. Our product candidates are in various stages of development and are subject to the risks of failure inherent in drug development. We have not submitted an application for or received marketing approval for any of our product candidates in the United States or in any other jurisdiction. We have limited experience in conducting and managing the clinical trials necessary to obtain marketing approvals, including FDA approval of an NDA.

The process of obtaining marketing approvals, both in the United States and abroad, is lengthy, expensive and uncertain. It may take many years, if approval is obtained at all, and can vary substantially based upon a

variety of factors, including the type, complexity and novelty of the product candidates involved. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. The FDA or other regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

In addition, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we, or any future collaborators, ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable. In addition, to the extent that we seek to develop a combination drug-device product for delivery of a product candidate or we rely on a previously cleared device to deliver a product candidate, we will also be dependent on FDA clearance or approval of such products.

Any delay in obtaining or failure to obtain required approvals and clearances could negatively impact our ability or that of any future collaborators to generate revenue from the particular product candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad. Any approval we are granted for our product candidates in the United States would not assure approval of our product candidates in foreign jurisdictions.

In order to market and sell our products in the European Union and other foreign jurisdictions, we, and any future collaborators, must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, a product must be approved for reimbursement before the product can be approved for sale in that country. We, and any future collaborators, may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may file for marketing approvals but not receive necessary approvals to commercialize our products in any market.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and

sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could harm our business.

We, or any future collaborators, may not be able to obtain orphan drug designation or orphan drug exclusivity for our product candidates and, even if we do, that exclusivity many not prevent the FDA or the EMA from approving other competing products.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. The FDA has granted orphan drug designation to APL-2 for the treatment of PNH. We, or any future collaborators, may seek orphan drug designations for other product candidates and may be unable to obtain such designations.

Even if we, or any future collaborators, obtain orphan drug designation for a product candidate, such as is the case for APL-2 for the treatment of PNH, we, or they, may not be able to obtain orphan drug exclusivity for that product candidate. Generally, a product with orphan drug designation only becomes entitled to orphan drug exclusivity if it receives the first marketing approval for the indication for which it has such designation, in which case the FDA or the EMA will be precluded from approving another marketing application for the same drug for that indication for the applicable exclusivity period. The applicable exclusivity period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we, or any future collaborators, obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

On August 3, 2017, the Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Fast track designation for one or more of our product candidates may not actually lead to a faster development or regulatory review or approval process.

In December 2016, we received fast track designation for APL-2 for the treatment of PNH. If a product is intended for the treatment of a serious condition and nonclinical or clinical data demonstrate the potential to address unmet medical need for this condition, a product sponsor may apply for FDA fast track designation. Even though we have received fast track designation for APL-2 for the treatment of PNH, fast track designation does not ensure that we will receive marketing approval or that approval will be granted within any particular timeframe. We may not experience a faster development or regulatory review or approval process with fast rack

designation compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

Even if we, or any future collaborators, obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we manufacture and market our products, which could impair our ability to generate revenue.

Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any future collaborators, must therefore comply with requirements concerning advertising and promotion for any of our product candidates for which we or they obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we and any future collaborators will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, any future collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, assuming we, or any future collaborators, receive marketing approval for one or more of our product candidates, we, and any future collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, and any future collaborators, are not able to comply with post-approval regulatory requirements, we, and any future collaborators, could have the marketing approvals for our products withdrawn by regulatory authorities and our, or any future collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Any of our product candidates for which we, or any future collaborators, obtain marketing approval in the future could be subject to post-marketing restrictions or withdrawal from the market and we, or any future collaborators, may be subject to substantial penalties if we, or they, fail to comply with regulatory requirements or if we, or they, experience unanticipated problems with our products following approval.

Any of our product candidates for which we, or any future collaborators, obtain marketing approval, as well as the manufacturing processes, post-approval studies and measures, labeling, advertising and promotional activities for such product, among other things, will be subject to ongoing requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a Risk Evaluation and Mitigation Strategy.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. The FDA and other agencies, including the Department of Justice,

closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we, or any future collaborators, do not market any of our product candidates for which we, or they, receive marketing approval for only their approved indications, we, or they, may be subject to warnings or enforcement action for off-label marketing. Violation of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

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

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- restrictions on coverage by third-party payors;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Current and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been and continue to be a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved products.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA. Among the provisions of the ACA of potential importance to our business and our product candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (and 70% starting January 1, 2019) point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2027 unless additional congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

With enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, among other things, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount

that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". Further, each chamber of the Congress has put forth multiple bills designed to repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA. The Congress will likely consider other legislation to replace elements of the ACA, during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the ACA exchanges. At the same time, the Administration announced that it will discontinue the payment of cost-sharing reduction, or CSR, payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA.

A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain. We will continue to evaluate the effect that the ACA and its possible repeal and replacement could have on our business.

The costs of prescription pharmaceuticals has also been the subject of considerable discussion in the United States, and members of Congress and the Administration have stated that they will address such costs through new legislative and administrative measures. To date, there have been several recent U.S. congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

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

Our relationships with customers and third-party payors, among others, will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to penalties,

including criminal sanctions, civil penalties, contractual damages, reputational harm, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of our operations, and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our current and future arrangements with healthcare providers, and third-party payors and customers, if any, will subject us to broadly applicable fraud and abuse and other healthcare laws and regulations. The laws and regulations may constrain the business or financial arrangements and relationships through which we conduct clinical research, market, sell and distribute any products for which we obtain marketing approval. These include the following:

Anti-Kickback Statute. The federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease or order of a good, facility, item or service for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

False Claims Laws. The federal false claims and civil monetary penalties laws, including the federal civil False Claims Act, impose criminal and civil penalties, including through civil whistleblower or *qui tam* actions against individuals or entities for, among other things, knowingly presenting or causing to be presented false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties;

HIPAA. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for, among other things, executing a scheme, or making materially false statements in connection with the delivery of or payment for health care benefits, items, or services. Additionally, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations on covered entities and their business associates that perform certain functions or activities that involve the use or disclosure of protected health information on their behalf, including mandatory contractual terms and technical safeguards, with respect to maintaining the privacy, security and transmission of individually identifiable health information;

Transparency Requirements. The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or transfers of value made to physicians and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members; and

Analogous State and Foreign Laws. Analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, can apply to sales or marketing arrangements, and claims involving healthcare items or services reimbursed by non-governmental third-party payors, and are generally broad and are enforced by many different federal and state agencies as well as through private actions. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. Additionally, some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties, and our business generally, will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental

authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, individual imprisonment, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm, and the curtailment or restructuring of our operations. Defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain products outside of the United States and require us to develop and implement costly compliance programs.

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

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The Securities and Exchange Commission, or SEC, also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable

materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, such as the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we, or any future collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed.

Risks Related to Employee Matters and Managing Growth

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

We are highly dependent on the pharmaceutical research and development and business development expertise of our executive team, including Cedric Francois, M.D., Ph.D., our President and Chief Executive Officer, and Pascal Deschatelets, Ph.D., our Chief Operating Officer. The members of our executive team are employed "at will," meaning any of them may terminate his employment with us at any time with or without notice and for any reason or no reason. In the future, we may be dependent on other members of our management, scientific and development team.

Our ability to compete in the biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. Our industry has experienced a high rate of turnover of management personnel in recent years. If we lose one or more of our executive officers or other key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers or other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain marketing approval of and commercialize products successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key employees on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions.

We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by

other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified personnel, our ability to develop and commercialize our product candidates will be limited.

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

We are exposed to the risk that our employees, independent contractors, consultants, collaborators and contract research organizations may engage in fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable non-U.S. regulatory authorities, to provide accurate information to the FDA or comparable non-U.S. regulatory authorities, to comply with manufacturing standards we have established, to comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities, to report financial information or data accurately or to disclose unauthorized activities to us. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant criminal, civil and administrative sanctions including monetary penalties, damages, fines, disgorgement, individual imprisonment, and exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, reputational harm, and we may be required to curtail or restructure our operations.

We expect to expand our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of February 28, 2018, we had 39 employees. We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug manufacturing, clinical, regulatory affairs and sales, marketing and distribution. Our headquarters are located in Kentucky and we maintain additional offices in Massachusetts and California. To manage these growth activities and separation of offices, we must continue to implement and improve our managerial, operational and financial systems and continue to recruit and train additional qualified personnel. Our management may need to devote a significant amount of its attention to managing these growth activities. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations, retain key employees, or identify, recruit and train additional qualified personnel. Our inability to manage the expansion of our operations effectively may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If we are unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy, including the successful commercialization of our product candidates.

We may engage in acquisitions that could disrupt our business, cause dilution to our stockholders or reduce our financial resources.

In the future, we may enter into transactions to acquire other businesses, products or technologies. Because we have not made any acquisitions to date, our ability to do so successfully is unproven. If we do identify

suitable candidates, we may not be able to make such acquisitions on favorable terms, or at all. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our common stock or other equity securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and non-disruptive manner. Acquisitions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

Risks Related to Ownership of Our Common Stock and This Offering

An active trading market for our common stock may not be sustainable. If an active trading market is not sustained, our ability to raise capital in the future may be impaired.

Our shares began trading on the Nasdaq Global Select Market on November 9, 2017. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares may not be sustained, which could put downward pressure on the market price of our common stock and thereby affect your ability to sell shares you purchase in this offering. An inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and impair our ability to acquire other companies or technologies by using our shares as consideration.

If you purchase shares of common stock in this offering, you will suffer immediate dilution in the net tangible book value of your investment.

The public offering price of our common stock is substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. Based on the public offering price of $25.50 per share, you will experience immediate dilution of $20.48 per share, representing the difference between our as adjusted net tangible book value per share after giving effect to this offering and the public offering price. Furthermore, if the underwriters exercise their option to purchase additional shares or our previously issued options or warrants to acquire common stock at prices below the public offering price are exercised, you will experience further dilution. For additional information on the dilution that you will experience immediately after this offering, see the section titled “Dilution.”

The trading price of our common stock is highly volatile, which could result in substantial losses for purchasers of our common stock in this offering.

The trading price of our common stock has been, and is likely to continue to be, highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. During the period from November 9, 2017 to April 18, 2018, the closing sales price of our common stock ranged from a high of $30.00 per share to a low of $12.71 per share. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the public offering price and you may lose some or all of your investment. The market price for our common stock may be influenced by many factors, including:

- the timing and results of our ongoing and planned clinical trials of APL-2 and any other product candidates;

- the success of existing or new competitive products or technologies;
- regulatory actions with respect to our product candidates or our competitors' products and product candidates;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- commencement or termination of collaborations for our development programs;
- failure or discontinuation of any of our product candidates or development programs;
- results of clinical trials of product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results or development timelines;
- recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and our resources, which could harm our business.

We have broad discretion in the use of the net proceeds from this offering and may invest or spend the proceeds in ways with which you do not agree and in ways that may not yield a return on your investment.

Although we currently intend to use the net proceeds from this offering in the manner described in the section titled "Use of Proceeds" in this prospectus, our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. You will not have the opportunity to influence our decisions on how to use our net proceeds from this offering. The failure by our management to apply these funds effectively could result in financial losses that could harm our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company until December 31, 2022, or until such earlier time as we have more than $1.07 billion in annual revenue, the market value of our stock held by non-affiliates is more than $700 million or we issue more than $1 billion of non-convertible debt over a three-year period. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or SOX Section 404, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. In this prospectus, we have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive as a result of our reliance on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, we incur, and after we are no longer an "emerging growth company," we will further incur, significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We expect that we will need to hire additional accounting, finance and other personnel in connection with our efforts to comply with the requirements of being a public company and our management and other personnel will need to devote a substantial amount of time towards maintaining compliance with these requirements. These requirements will increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

Pursuant to SOX Section 404 we will be required to furnish a report by our management on our internal control over financial reporting beginning with our second filing of an Annual Report on Form 10-K with the SEC and after we are no longer an emerging growth company, we will be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with SOX Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

A significant portion of our total outstanding shares is restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common stock to decline significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. Following this offering, we will have 55,872,762 shares of common stock outstanding based on the 50,372,762 shares of our common stock outstanding as of February 28, 2018. Of these shares, approximately 38.5 million shares are currently restricted under securities laws or as a result of lock-up agreements with the representatives of the underwriters for our initial public offering or other agreements. The lock-up restrictions entered into in connection with the initial public offering are due to expire on May 6, 2018, resulting in these shares becoming eligible for public sale on May 7, 2018, subject to applicable securities laws. Additionally, approximately 13.7 million of the outstanding shares of our common stock will be subject to lock-up agreements entered into in connection with this offering but may be sold beginning 90 days after the date of this prospectus. The representatives of the underwriters for our initial public offering and for this offering may release stockholders from their lock-up agreements with the underwriters at any time and without notice, which would allow for earlier sales of shares in the public market. Any of our remaining shares, including the shares sold by us in this offering, may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act of 1933, as amended, or the Securities Act, or to the extent such shares were issued in our initial public offering and are held by nonaffiliates of ours.

In November 2017, we filed a registration statement registering all shares of common stock that we may issue under our equity compensation plans. As of February 28, 2018, we had options to purchase an aggregate of 7,396,674 shares of our common stock outstanding, of which options to purchase 3,373,956 shares were vested. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described above. Moreover, holders of an aggregate of 11,178,984 shares of our common stock will have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. If these additional shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law new legislation that significantly revises the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the newly enacted federal tax law. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

We might not be able to utilize a significant portion of our net operating loss carryforwards and research and development tax credit carryforwards.

As of December 31, 2017, we had both federal and state net operating loss carryforwards of $118.8 million, and federal research and development tax credit carryforwards of $8.3 million, all of which if not utilized will begin to expire in 2024. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the newly enacted federal income tax law, federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. We experienced a Section 382 ownership change in September 2015, which imposes annual limitations on our use of pre-change net operating loss carryforwards and other pre-change tax attributes. In addition, we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. We have determined that our research and development credit carryforwards are also limited. These limitations upon our historical net operating loss and tax credit carryforwards may harm our future operating results by effectively increasing our future tax obligations.

We do not anticipate paying any cash dividends on our capital stock in the foreseeable future. Accordingly, stockholders must rely on capital appreciation, if any, for any return on their investment.

We have never declared nor paid cash dividends on our capital stock. We currently plan to retain all of our future earnings, if any, to finance the operation, development and growth of our business. In addition, the terms of our term loan facility with Silicon Valley Bank precludes us from paying dividends, and any future debt or credit agreements may also preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

Concentration of ownership of our common stock among our existing executive officers, directors and principal stockholders may prevent new investors from influencing significant corporate decisions.

As of February 28, 2018, our executive officers and directors, and entities associated and affiliated with our executive officers and directors, in the aggregate, beneficially owned shares representing approximately 37.9% of our outstanding common stock before this offering, and our largest stockholder, Morningside Venture Investments, Ltd., beneficially owned approximately 22.5% of our outstanding common stock before this offering. If, as we expect, Potentia Holdings LLC distributes the shares of our common stock it holds to its stockholders at some point in the future, the percentage of our shares held by certain of our directors and executive officers who are stockholders of Potentia Holdings LLC will increase. As a result, if these stockholders were to choose to act together, they may have the ability to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, could substantially influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of ownership may:

- delay, defer or prevent a change in control;
- entrench our management or the board of directors; or
- impede a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

Some of these persons or entities may have interests different than yours. For example, because many of these stockholders purchased their shares at prices substantially below the price at which shares are being sold in

this offering and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors or they may want us to pursue strategies that deviate from the interests of other stockholders.

Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management or hinder efforts to acquire a controlling interest in us.

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that all members of the board are not elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on at stockholder meetings;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call a special meeting of stockholders;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a “poison pill” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. This could discourage, delay or prevent someone from acquiring us or merging with us, whether or not it is desired by, or beneficial to, our stockholders. This could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

The trading market for our common stock will likely depend in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. There can be no assurance that analysts will continue to cover us or provide favorable coverage. Securities or industry analysts may elect not to provide research coverage of our common stock, and such lack of research coverage may negatively impact the market price of our common stock. In the event we do have analyst coverage, if one or more analysts downgrade our stock or change their opinion of our stock, our share price

would likely decline. In addition, if one or more analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

Our restated certificate of incorporation designates the state courts in the State of Delaware or, if no state court located within the State of Delaware has jurisdiction, the federal court for the District of Delaware, as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could discourage lawsuits against our company and our directors, officers and employees.

Our restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or employees to our company or our stockholders, any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our restated certificate of incorporation or amended and restated bylaws, or any action asserting a claim against us governed by the internal affairs doctrine. This exclusive forum provision may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this prospectus, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management and expected market growth are forward-looking statements. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These forward-looking statements include, among other things, statements about:

- our plans with respect to our ongoing and planned clinical trials for our product candidates, whether conducted by us or by any future collaborators, including the timing of these trials and of the anticipated results;
- our plans to initiate clinical trials of APL-2;
- the potential clinical benefits and attributes of APL-2 and the inhibition of C3;
- our plans to develop APL-2 for any additional indications;
- our plans to research, develop and commercialize our current and future product candidates;
- our plans to potentially seek to enter into collaborations for the development and commercialization of certain product candidates;
- the potential benefits of any future collaboration;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of any products for which we receive marketing approval;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position and strategy;
- our ability to identify additional products or product candidates with significant commercial potential;
- our expectations related to the use of proceeds from this offering;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- developments relating to our competitors and our industry; and
- the impact of government laws and regulations.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus, particularly in the “Risk Factors” section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or enter into.

You should read this prospectus and the documents that we have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

This prospectus includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. All of the market data used in this prospectus involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. We believe that the information from these industry publications, surveys and studies is reliable. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of important factors, including those described in the section titled “Risk Factors.” These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of 5,500,000 shares of our common stock in this offering will be $131.3 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that the net proceeds to us from this offering will be approximately $151.1 million.

As of December 31, 2017, we had cash and cash equivalents of $175.6 million. We currently estimate that we will use the net proceeds from this offering, together with our existing cash and cash equivalents, as follows:

- approximately $126.0 million for our ongoing and planned clinical trials of APL-2 in patients with GA and wet AMD;
- approximately $95.0 million for our ongoing and planned clinical trials of APL-2 in patients with PNH;
- approximately $58.0 million for our other planned clinical trials of APL-2 and development of new product candidates; and
- the remainder for working capital and other general corporate purposes.

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements at least through into the third quarter of 2019. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

We do not expect that the net proceeds from this offering and our existing cash and cash equivalents will be sufficient to enable us to complete our planned Phase 3 clinical trials of APL-2 or to complete the development of APL-2 or any of our other product candidates.

This expected use of the net proceeds from this offering and our existing cash and cash equivalents represents our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development and commercialization efforts, the status of and results from clinical trials, any collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering. We have no current agreements, commitments or understandings for any material acquisitions or licenses of any products, businesses or technologies.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in money market funds, government-insured bank deposit accounts or U.S. government securities.

MARKET PRICE OF COMMON STOCK

Our common stock commenced trading on the Nasdaq Global Select Market under the symbol “APLS” on November 9, 2017. Prior to that date, there was no public trading market for our common stock. The following table sets forth, for the periods indicated, the high and low reported sales prices of our common stock as reported on the Nasdaq Global Select Market from November 9, 2017 to April 18, 2018:

	High	Low
Year Ended December 31, 2017		
Fourth Quarter (from November 9, 2017)	$24.17	$12.45
Year Ending December 31, 2018		
First Quarter	$27.53	$13.54
Second Quarter (through April 18, 2018)	$32.00	$19.24

The last reported sale price of our common stock on the Nasdaq Global Select Market on April 18, 2018 was $26.37 per share. As of February 28, 2018, there were 112 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

DIVIDEND POLICY

We have never declared nor paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, our term loan facility with Silicon Valley Bank contains restrictive covenants that prohibit us, subject to certain exceptions, from paying dividends on our common stock, and future debt securities or other financing arrangements could contain similar or more restrictive negative covenants. We do not intend to pay cash dividends in respect of our common stock in the foreseeable future.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and our capitalization as of December 31, 2017 on:

- an actual basis; and
- an as adjusted basis to give effect to our issuance and sale of 5,500,000 shares of common stock in this offering at a public offering price of $25.50 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

Our capitalization following the closing of this offering will depend on the actual number of shares sold, the public offering price and other terms of this offering determined at pricing. You should read this table together with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and the related notes appearing elsewhere in this prospectus.

	As of December 31, 2017	
	Actual	As Adjusted
	(in thousands)	
Cash and cash equivalents	$ 175,644	$ 306,979
Term loan facility	$ 19,807	$ 19,807
Promissory note—related party	6,583	6,583
Common stock warrant liability	244	244
Stockholders' equity (deficit)		
Preferred stock, $0.0001 par value; 10,000,000 shares authorized and no shares issued or outstanding, actual and as adjusted	—	—
Common stock, $0.0001 par value; 200,0000,000 shares authorized, actual and as adjusted; 50,334,152 shares issued and outstanding, actual; 55,834,152 shares issued and outstanding as adjusted	5	6
Additional paid-in capital	298,201	429,536
Accumulated deficit	(149,263)	(149,263)
Total stockholders' equity	148,943	280,278
Total capitalization	$ 175,577	$ 306,912

The table above does not include:

- 6,355,581 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2017, at a weighted-average exercise price of $4.78 per share;
- 1,126,585 shares of our common stock issuable upon the exercise of stock options granted after December 31, 2017, at a weighted average exercise price of $15.13 per share;
- 1,682,596 and 468,823 additional shares of our common stock available for future issuance, as of December 31, 2017, under our 2017 stock incentive plan and our 2017 employee stock purchase plan, respectively, as well as any automatic increases in the number of shares of common stock reserved under these plans; and
- 14,064 shares of our common stock issuable upon the exercise of warrants outstanding as of December 31, 2017, at an exercise price of $5.484 per share.

DILUTION

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

Our historical net tangible book value as of December 31, 2017 was $148.9 million, or $2.96 per share of our common stock. Our historical net tangible book value is the amount of our total tangible assets less our total liabilities. Historical net tangible book value per share represents our historical net tangible book value divided by the 50,334,152 shares of our common stock outstanding as of December 31, 2017.

Investors participating in this offering will incur immediate and substantial dilution. After giving further effect to our issuance and sale of 5,500,000 shares of our common stock in this offering at a public offering price of $25.50 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2017 would have been $280.2 million, or $5.02 per share. This represents an immediate increase in as adjusted net tangible book value per share of $2.06 to existing stockholders and immediate dilution of $20.48 in as adjusted net tangible book value per share to new investors purchasing shares of our common stock in this offering. Dilution per share to new investors is determined by subtracting as adjusted net tangible book value per share after this offering from the public offering price per share paid by new investors.

The following table illustrates this dilution:

Public offering price per share		$25.50
Historical net tangible book value per share as of December 31, 2017	$2.96	
Increase in net tangible book value per share attributable to new investors purchasing shares of our common stock in this offering	2.06	
As adjusted net tangible book value per share immediately after this offering		5.02
Dilution per share to new investors		$20.48

The table above excludes:

- 6,355,581 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2017, at a weighted-average exercise price of $4.78 per share;
- 1,126,585 shares of our common stock issuable upon the exercise of stock options granted after December 31, 2017, at a weighted average exercise price of $15.13 per share;
- 1,682,596 and 468,823 additional shares of our common stock available for future issuance, as of December 31, 2017, under our 2017 stock incentive plan and our 2017 employee stock purchase plan, respectively, as well as any automatic increases in the number of shares of common stock reserved under these plans; and
- 14,064 shares of our common stock issuable upon the exercise of warrants outstanding as of December 31, 2017, at an exercise price of $5.484 per share.

To the extent that the underwriters exercise their option to purchase additional shares, stock options or warrants are exercised, new stock options are issued under our equity incentive plans, or we issue additional shares of common stock in the future, there will be further dilution to investors participating in this offering. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

SELECTED CONSOLIDATED FINANCIAL DATA

You should read the following selected consolidated financial data together with our consolidated financial statements and the related notes appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus. We have derived the statement of operations data for the years ended December 31, 2015, 2016 and 2017 and the balance sheet data as of December 31, 2015, 2016 and 2017 from our audited consolidated financial statements appearing at the end of this prospectus. In the opinion of management, the unaudited condensed consolidated financial data reflects all adjustments, consisting only of normal recurring adjustments, necessary for a fair presentation of the financial information as of and for the periods presented. Our historical results are not necessarily indicative of results that should be expected in any future period.

	Year Ended December 31,		
	2015	2016	2017
Consolidated Statement of Operations Data:			
Operating expenses:			
Research and development	$ 13,730,311	$ 22,978,599	$ 40,303,878
Cost of acquired in-process research and development	26,486,000	—	—
General and administrative	6,356,782	4,303,743	10,463,151
Operating loss	(46,573,093)	(27,282,342)	(50,767,029)
Loss from remeasurement of fair value of warrant	—	—	(153,692)
Interest income (expense), net(1)	50,853	135,309	(96,915)
Other income, net	6,284	22,396	11,542
Net loss and comprehensive loss	$ (46,515,956)	$ (27,124,637)	$ (51,006,094)
Net loss per share, basic and diluted(2)	$ (8.03)	$ (3.22)	$ (3.68)
Weighted-average number of shares used in net loss per share, basic and diluted	5,795,040	8,428,366	13,870,949

(1) Includes amortization of debt discount associated with term loan facility and promissory note due to the issuance of warrants. See Notes 6 and 7 to our audited consolidated financial statements included elsewhere in this prospectus.

(2) See Note 13 in the notes to our audited consolidated financial statements appearing at the end of this prospectus for a description of the method used to calculate basic and diluted net loss per common share.

	As of December 31,		
	2015	2016	2017
Consolidated Balance Sheet Data:			
Cash and cash equivalents	$ 36,003,546	$ 24,863,488	$ 175,643,529
Working capital	34,843,678	23,729,792	175,461,348
Total assets	38,177,109	27,433,258	182,131,456
Term loan facility	—	—	19,806,944
Promissory note related party	—	—	6,583,402
Total liabilities	3,200,160	3,638,938	33,188,596
Convertible preferred stock	77,191,906	92,054,926	—
Accumulated deficit	(71,132,922)	(98,257,559)	(149,263,653)
Total stockholders' equity	34,976,949	23,794,320	148,942,860

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

You should read the following discussion and analysis of our financial condition and results of operations together with the section of this prospectus titled "Selected Consolidated Financial Data" and our consolidated financial statements and related notes included elsewhere in this prospectus. This discussion and other parts of this prospectus contain forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations and intentions. As a result of many factors, including those factors set forth in the "Risk Factors" section of this prospectus, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical-stage biopharmaceutical company focused on the development of novel therapeutic compounds to treat disease through the inhibition of the complement system, which is an integral component of the immune system, at the level of C3, the central protein in the complement cascade. We believe that this approach can result in broad inhibition of the principal pathways of the complement system and has the potential to effectively control a broad array of complement-dependent autoimmune and inflammatory diseases.

We have the most advanced clinical program targeting C3. We believe that our lead product candidate, APL-2, has the potential to be a best-in-class treatment that may address the limitations of existing treatment options or provide a treatment option where there currently is none. APL-2 has already shown activity that we believe is clinically meaningful in clinical trials for two distinct medical conditions—geographic atrophy in age-related macular degeneration, or GA, and paroxysmal nocturnal hemoglobinuria, or PNH—and we plan to conduct clinical trials in additional complement-dependent diseases. In our Phase 2 clinical trial of APL-2 in patients with GA, treatment with APL-2 resulted in a significant reduction in the rate of GA lesion growth over 12 months, and we are planning to initiate a Phase 3 clinical program evaluating APL-2 in patients with GA. In our two ongoing Phase 1b clinical trials in PNH, APL-2 achieved improvements in transfusion dependency, hemoglobin levels and other hematological indicators that we believe are clinically meaningful. We are also developing other novel compounds targeting C3. We hold worldwide commercialization rights to APL-2 and these other novel compounds targeting C3.

Since our commencement of operations in May 2010, we have devoted substantially all of our resources to developing our proprietary technology, developing product candidates, undertaking preclinical studies and conducting clinical trials for APL-2, building our intellectual property portfolio, organizing and staffing our company, business planning, raising capital, and providing general and administrative support for these operations.

On November 13, 2017, we issued and sold 10,714,000 shares of common stock in our initial public offering or IPO, at a price to the public of $14.00 per share for net proceeds of $137.2 million after deducting underwriting discounts and commissions of $10.5 million and offering expenses of approximately $2.3 million. In addition, on December 13, 2017, we issued and sold an additional 981,107 shares of common stock at a price to the public of $14.00 per share pursuant to the underwriters' partial exercise of their over-allotment option, for net proceeds of approximately $12.8 million, after underwriting discounts and commissions. On November 13, 2017, upon the closing of the IPO, all shares of redeemable convertible preferred stock then outstanding converted into an aggregate of 30,070,034 shares of common stock.

To date, we have financed our operations primarily through $149.9 million in net proceeds from the IPO, $112.6 million in proceeds from the private placement of shares of our convertible preferred stock, $20.0 million in proceeds from borrowings under our term loan facility with Silicon Valley Bank, and $7.0 million in proceeds from our issuance and sale of a promissory note to an affiliate of one of our stockholders.

In September 2015, we acquired the assets of Potentia Pharmaceuticals, Inc., or Potentia, pursuant to an asset purchase agreement with Potentia. The acquired assets consist primarily of a license agreement with the University of Pennsylvania, or Penn, that was assigned to us. This license agreement with Penn provides us with an exclusive license, under specified patent rights controlled by Penn, to develop and commercialize products covered by the licensed patent rights for ophthalmic indications. Upon the closing of the asset acquisition, we issued 3,844,352 shares of our common stock to Potentia, and incurred an in-process research and development expense of $26.5 million. Certain of our directors and officers are directors, officers and stockholders of Potentia. See "Transactions with Related Persons" for more information.

We have not generated any revenue from product sales. We have incurred significant annual net operating losses in each year since our inception and expect to continue to incur net operating losses for the foreseeable future. Our net losses were $46.5 million, 27.1 million and $51.0 million for the years ended December 31, 2015, 2016 and 2017, respectively. As of December 31, 2017, we had an accumulated deficit of $149.3 million. We expect to continue to incur significant expenses and increasing operating losses for the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase significantly if and as we continue to develop and conduct clinical trials in our current and new indications with APL-2, including our planned Phase 3 trials in GA and PNH; initiate and continue research and preclinical and clinical development efforts for any future product candidates; seek to identify and develop additional product candidates for complement-dependent diseases; seek regulatory and marketing approvals for our product candidates that successfully complete clinical trials, if any; establish sales, marketing, distribution and other commercial infrastructure in the future to commercialize any products for which we may obtain marketing approval; require the manufacture of larger quantities of product candidates for clinical development and, potentially, commercialization; maintain, expand and protect our intellectual property portfolio; hire and retain additional personnel, such as clinical, quality control and scientific personnel; add operational, financial and management information systems and personnel, including personnel to support our product development and help us comply with our obligations as a public company; and add equipment and physical infrastructure to support our research and development programs. In addition, we expect to incur additional costs associated with operating as a public company.

As of December 31, 2017, we had cash and cash equivalents of $175.6 million. Without giving effect to the anticipated net proceeds from this offering, we do not believe that those cash and cash equivalents will be sufficient to enable us to fund our current operations for longer than 12 months from the date of this prospectus and have therefore concluded that this circumstance raises substantial doubt about our ability to continue as a going concern. See Note 1 to our consolidated financial statements appearing elsewhere in this prospectus for additional information on our assessment. We believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements at least through .

Financial Operations Overview

Revenue

We have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the near future. In the future, we will seek to generate revenue primarily from a combination of product sales and collaborations with strategic partners.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts, and the development of our product candidates, which include:

- employee-related expenses including salaries, bonuses, benefits and share-based compensation expense;

- expenses incurred under agreements with third parties, including contract research organizations, or CROs, that conduct clinical trials and research and development activities on our behalf, and contract manufacturing organizations that manufacture quantities of drug supplies for both our preclinical studies and clinical trials;
- the cost of consultants, including share-based compensation expense; and
- various other expenses incident to the management of our preclinical studies and clinical trials.

Research and development costs are expensed as incurred. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed. We have not provided program costs since inception because historically we have not tracked or recorded our research and development expenses on a program-by-program basis.

The following summarizes our most advanced research and development programs:

- ***GA***. We are developing APL-2 as monotherapy for GA, administered by intravitreal injections. In our Phase 2 clinical trial of APL-2 in patients with GA, treatment with APL-2 resulted in a significant reduction in the rate of GA lesion growth at 12 months compared to sham. We plan to initiate Phase 3 clinical trials of APL-2 in GA in the second half of 2018 and to initiate a Phase 1b/2 trial of APL-2 in patients with wet AMD in the second quarter of 2018.
- ***PNH***. We are developing APL-2 as monotherapy for patients with PNH, administered by subcutaneous injection. In our ongoing Phase 1b clinical trials of APL-2 in patients being treated with eculizumab and in treatment-naïve patients, APL-2 treatment was associated with improvements in transfusion dependency, hemoglobin levels and other hematological indicators that we believe are clinically meaningful. We plan to initiate a Phase 3 clinical trial in patients with PNH in the second half of 2018.

We also plan to initiate a Phase 2 clinical trial of APL-2 in patients with autoimmune hemolytic anemia in the first half of 2018 and a Phase 2 clinical trial of APL-2 in patients with complement-dependent nephropathies in the first half of 2018.

The successful development of our product candidates is highly uncertain. Accordingly, at this time, we cannot reasonably estimate the nature, timing and costs of the efforts that will be necessary to complete the remainder of the development of these product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from APL-2 or any other potential product candidates. This is due to the numerous risks and uncertainties associated with developing therapeutics, including the uncertainties of:

- establishing an appropriate safety profile in preclinical studies;
- successful enrollment in, and completion of clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- launching commercial sales of the products, if and when approved, whether alone or in collaboration with others; and
- an acceptable safety profile of the products following approval.

A change in the outcome of any of these variables with respect to the development of any of our product candidates would significantly change the costs and timing associated with the development of that product candidate.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect research and development costs to increase significantly for the foreseeable future as our product candidate development programs progress. However, we do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. There are numerous factors associated with the successful commercialization of any of our product candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control will impact our clinical development programs and plans.

General and Administrative Expenses

General and administrative expenses consist primarily of employee-related expenses including salaries, bonuses, benefits and share-based compensation. Other significant costs include facility costs not otherwise included in research and development expenses, legal fees relating to patent and corporate matters, and fees for accounting and consulting services.

We anticipate that our general and administrative expenses will increase in the future to support continued research and development activities, potential commercialization of our product candidates and increased costs of operating as a public company. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, attorneys and accountants, among other expenses. Additionally, we anticipate increased costs associated with being a public company including expenses related to services associated with maintaining compliance with exchange listing and SEC requirements, insurance costs and investor relations costs.

Loss From Remeasurement of Fair Value of Warrants

Loss from remeasurement of fair value of warrants consists of losses from the remeasurement of the fair value of our liabilities related to the common stock warrants that we issued to Silicon Valley Bank on October 20, 2017. Prior to our IPO, these warrants were exercisable into shares of common stock that were contingently redeemable in certain circumstances. As such, we classified these warrants as liabilities in the consolidated balance sheet at their estimated fair values at issuance, and we recorded the change in the estimated fair values at December 31, 2017 as loss from remeasurement of fair value of warrants during the year ended December 31, 2017.

Critical Accounting Policies and Estimates

This discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported amounts of expenses during the reporting periods. On an ongoing basis, we evaluate our estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our financial statements included elsewhere in this prospectus, we believe that the following accounting policies are the most critical to aid you in fully understanding and evaluating our financial condition and results of operations.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing quotations and contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by CROs and contract manufacturing organizations, or CMOs, in connection with research and development activities for which we have not yet been invoiced.

We base our expenses related to CROs and CMOs on our estimates of the services received and efforts expended pursuant to quotes and contracts with CROs and CMOs. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our CROs and CMOs will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting expense amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Share-Based Compensation

We measure share-based awards granted to employees, consultants and members of the board of directors at fair value on the date of grant and recognize the corresponding share-based compensation expense of those awards, net of forfeitures, over the requisite service period, which is generally the vesting period of the respective award. We have historically granted stock options with exercise prices equivalent to the fair value of our common stock, with reference to arms' length transactions effected contemporaneously with the date of grant of the stock options.

We measure other share-based awards granted to non-employees at fair value as of the end of each reporting period and record expense for the awards over the period in which the related services are rendered.

We estimated the fair value of each stock option grant using the Monte Carlo simulation model, or Monte Carlo, for grants made on or prior to June 30, 2015 and the Black-Scholes option pricing model, or Black-Scholes, for grants made on or after July 1, 2015. We historically have been a privately-held company and lack company-specific historical and implied volatility information. Therefore, we estimate our expected volatility based on the historical volatility of a representative group of publicly traded biopharmaceutical companies and expect to continue to do so until we have adequate historical data regarding the volatility of our traded stock price. We determine the expected term of our options utilizing the probability weighted time to liquidity event at each grant date, assuming that holders of our options will exercise at the time of such liquidity event. We determine the risk-free interest rate by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. We assume an expected dividend yield of zero because we have never paid cash dividends and do not expect to pay any cash dividends in the foreseeable future.

Valuations of Common Stock

Due to the absence of a public trading market for our common stock, since inception through November 9, 2017, which is the date our common stock commenced trading on the Nasdaq Global Select Market, our retrospective and contemporaneous determinations of the fair value of our common stock were performed using methodologies, approaches and assumptions consistent with the American Institute of Certified Public Accountants Audit and Accounting Practice Aid Series: *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. There are significant judgments and estimates inherent in the determination of the fair value of our common stock, including the contemporaneous and retrospective valuations. These judgments and estimates include assumptions regarding our future operating performance, the probability and timing of completing an initial public offering or other liquidity event and the determinations of the appropriate valuation methods. If we had made different assumptions, our share-based compensation expense, net loss and net loss per share could have been significantly different.

Since the IPO, we have determined the fair market value of our common stock using the market closing price of our common stock as reported on the Nasdaq Global Select Market.

Valuation Methodologies

Prior to our IPO, the common stock valuations were prepared using a hybrid of the option-pricing method, or OPM, and the probability-weighted expected return method, or PWERM.

OPM. The OPM treats each class of common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceed the value of the preferred stock liquidation preference at the time of a liquidity event, such as a strategic sale, merger or initial public offering. The common stock is modeled as a call option on the underlying equity value at a predetermined exercise price. In the model, the exercise price is based on a comparison with the total equity value rather than, as in the case of a regular call option, a comparison with a per share stock price. Thus, common stock is considered to be a call option with a claim on the enterprise at an exercise price equal to the remaining value immediately after the preferred stock liquidation preference is paid.

The OPM uses Monte Carlo or Black-Scholes to price the call options. This model defines the securities' fair values as functions of the current fair value of a company and uses assumptions such as the anticipated timing of a potential liquidity event and the estimated volatility of the equity securities. The aggregate value of the common stock derived from the OPM is then divided by the number of shares of common stock outstanding to arrive at the per share value.

We used the OPM backsolve approach to estimate enterprise value under the OPM. The OPM backsolve approach uses the OPM to calculate the implied equity value based on recent sales of the company's securities. For the OPM, we based our assumed volatility factor on the historical trading volatility of our publicly traded peer companies. For each valuation date, we determined the appropriate volatility to be used, considering such factors as our expected time to a liquidity event and our stage of development.

To derive the fair value of our common stock using the OPM, we calculated the proceeds to the common stockholders based on the preferences and priorities of the preferred and common stock. We then applied a discount for lack of marketability to the common stock to account for the lack of access to an active public market.

PWERM. The PWERM is a scenario-based methodology that estimates the fair value of common stock based upon an analysis of future values for the company, assuming various outcomes. The common stock value

is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of stock. The future value of the common stock under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common stock. A discount for lack of marketability is then applied to the common stock to account for the lack of access to an active public market.

JOBS Act

In April 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an "emerging growth company," or EGC, can take advantage of the extended transition period for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

We are in the process of evaluating the benefits of relying on other exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an EGC, we intend to rely on certain of these exemptions, including exemptions from the requirement to provide an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and from any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis. We will remain an EGC until the earlier of: the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more; the last day of 2022; the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years; or the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

Results of Operations

Comparison of Years Ended December 31, 2016 and 2017

The following table summarizes our results of operations for the years ended December 31, 2016 and 2017, together with the dollar increase or decrease and percentage change in those items:

	Year Ended December 31,		Change	Change
	2016	2017	$	%
Operating expenses:				
Research and development	$ 22,978,599	$ 40,303,878	$ 17,325,279	75.4%
General and administrative	4,303,743	10,463,151	6,159,408	143.1
Operating loss	(27,282,342)	(50,767,029)	(23,484,687)	86.1
Loss from remeasurement of fair value of warrants	—	(153,692)	(153,692)	100.0
Interest income (expense), net	135,309	(96,915)	(232,224)	(171.6)
Other income, net	22,396	11,542	(10,854)	(48.5)
Net loss and comprehensive loss	$(27,124,637)	$(51,006,094)	$(23,881,457)	88.0

Research and Development Expenses

The following table summarizes our research and development expenses incurred during the years ended December 31, 2016 and 2017, together with the dollar increase or decrease and percentage change in those items:

	Year Ended December 31,		Change	Change
	2016	2017	$	%
Clinical trial costs	$11,486,499	$15,231,683	$ 3,745,184	32.6%
Contract manufacturing	5,098,538	13,323,343	8,224,805	161.3
Pre-clinical study expenses	3,431,482	1,699,902	(1,731,580)	(50.5)
Compensation and related personnel costs	1,989,164	4,933,207	2,944,043	148.0
Other research and development costs	972,916	3,659,506	2,686,590	276.1
Device development expenses	—	1,456,238	1,456,238	100.0
Total research and development expenses	$22,978,599	$40,303,878	$17,325,279	75.4

Research and development expenses increased by $17.3 million to $40.3 million for the year ended December 31, 2017 from $23.0 million for the year ended December 31, 2016, an increase of 75.4%. The increase in research and development expenses was primarily attributable to an increase of $8.2 million in manufacturing expenses, an increase of $3.7 million in clinical trial costs, an increase of $2.9 million in employee related costs primarily due to the hiring of additional personnel, an increase of $2.7 million related to research and development supporting activities, and an increase of $1.5 million in device development expenses, partially offset by a decrease of $1.7 million in preclinical study expenses.

General and Administrative Expenses

General and administrative expenses increased by $6.2 million to $10.5 million for the year ended December 31, 2017, from $4.3 million for the year ended December 31, 2016, an increase of 143.1%. The increase in general and administrative expenses was primarily attributable to an increase in employee related costs of $3.8 million, an increase in professional and consulting fees of $1.5 million, and an increase in office, travel and related costs of $0.9 million. The increased employee related costs of $3.8 million consisted of $1.6 million related to an increase in salaries and benefits primarily due to the hiring of additional members of our management team, $1.8 million related to stock option expense associated with the grants of stock options to the members of our board of directors upon the IPO, and $0.5 million in recruitment expense. The increased professional and consulting fees of $1.5 million primarily consisted of an increase in consulting fees of $1.0 million, an increase of $0.4 million in legal fees and an increase of $0.1 million in accounting fees.

Loss From Remeasurement of Fair Value of Warrants

Loss from remeasurement of fair value of warrants was $0.2 million for the year ended December 31, 2017, an increase of $0.2 million compared to the year ended December 31, 2016. The increase was due to the remeasurement of the fair value of our liabilities related to the common stock warrants that we issued to Silicon Valley Bank on October 20, 2017. At December 31, 2016, there was no obligation related to the future issuance of our common stock and therefore no common stock derivative liability on the consolidated balance sheets.

Interest Income (Expense), Net

Interest income (expense), net was an expense of $0.1 million for the year ended December 31, 2017, a decrease of $0.2 million, compared to $0.1 million of interest income for the year ended December 31, 2016. The interest expense incurred in 2017 was primarily attributable to interest expense incurred on our long-term debt. The interest income earned in 2016 and 2017 relates to interest earned from cash equivalents and cash equivalents.

Other Income, Net

Other income, net remained relatively stable for the year ended December 31, 2017 as compared to the year ended December 31, 2016. In both periods, other income was primarily attributable to rent charged to two related entities while other expense was primarily related to corporate franchise taxes and fees.

Comparison of Years Ended December 31, 2015 and 2016

The following table summarizes our results of operations for the years ended December 31, 2015 and 2016, together with the dollar increase or decrease and percentage change in those items:

	Year Ended December 31,		Change	Change
	2015	2016	$	%
Operating expenses:				
Research and development	$ 13,730,311	$ 22,978,599	$ 9,248,288	67.4%
Cost of acquired in process research and development	26,486,000	—	(26,486,000)	(100.0)
General and administrative	6,356,782	4,303,743	(2,053,039)	(32.3)
Operating loss	(46,573,093)	(27,282,342)	19,290,751	(41.4)
Interest income, net	50,853	135,309	84,456	166.1
Other income, net	6,284	22,396	16,112	256.4
Net loss and comprehensive loss	$(46,515,956)	$(27,124,637)	$ 19,391,319	(41.7)

Research and Development Expenses

The following table summarizes our research and development expenses incurred during the years ended December 31, 2015 and 2016, together with the dollar increase or decrease and percentage change in those items:

	Year Ended December 31,		Change	Change
	2015	2016	$	%
Clinical trial costs	$ 6,926,701	$11,486,499	$4,559,798	65.8%
Contract manufacturing	1,969,963	5,098,538	3,128,575	158.8
Pre-clinical study expenses	3,466,671	3,431,482	(35,189)	(1.0)
Compensation and related personnel costs	1,160,379	1,989,164	828,785	71.4
Other research and development costs	206,597	972,916	766,319	370.9
Total research and development expenses	$13,730,311	$22,978,599	$9,248,288	67.4

Research and development expenses increased by $9.2 million to $23.0 million for the year ended December 31, 2016 from $13.7 million for the year ended December 31, 2015, an increase of 67.4%. The increase was attributable to an increase of $4.6 million in clinical trial costs, an increase of $3.1 million in formulation and manufacturing expenses, an increase of $0.8 million in employee related costs as a result of hiring additional personnel and an increase of $0.7 million related to other research and development costs for supporting activities.

Cost of Acquired In-Process Research and Development

We incurred $26.5 million in acquired in-process research and development expenses during the year ended December 31, 2015. We incurred this cost in connection with the closing in September 2015 of the asset purchase agreement that we entered into with Potentia in September 2014, as we valued the 3,884,352 shares of our common stock that we issued to Potentia upon the closing at $26.5 million. We allocated the entire purchase price to acquired in-process research and development. We had no acquired in-process research and development expenses during the year ended December 31, 2016.

General and Administrative Expenses

General and administrative expenses decreased by $2.1 million to $4.3 million for the year ended December 31, 2016 from $6.4 million for the year ended December 31, 2015, a decrease of 32.3%. The decrease was attributable to a $2.0 million write-off of deferred issuance costs related to our efforts to conduct an initial public offering in 2015 and 2016 that we ended in February 2016, a $0.4 million decrease in consulting expense associated with finance and accounting, and a $0.2 million decrease in intellectual property legal fees. These decreases were offset by increased employee costs of $0.4 million and increased professional and consulting fees of $0.1 million.

Interest Income

Interest income for the years ended December 31, 2015 and 2016 relates to interest earned from cash and cash equivalents.

Other Income, Net

Other income, net remained relatively stable for the year ended December 31, 2016, as compared to the year ended December 31, 2015. In both periods, other income was primarily attributable to rent charged to two related entities while other expense was primarily attributable to corporate franchise taxes and fees.

Liquidity and Capital Resources

Sources of Liquidity

Since inception, we have financed our operations primarily through $149.9 million in proceeds from our IPO, $112.6 million in proceeds from the private placement of shares of our convertible preferred stock, $20.0 million in proceeds from borrowings under our term loan facility with Silicon Valley Bank, and $7.0 million in proceeds from our issuance and sale of a promissory note to an affiliate of one of our stockholders.

Indebtedness

On October 20, 2017, we entered into a loan and security agreement with Silicon Valley Bank providing for a $20.0 million term loan facility, which we refer to as the term loan facility.

Borrowings under the term loan facility bear interest at a floating rate per annum equal to the WSJ prime rate plus 1.50%. In an event of default, as defined in the loan and security agreement, the interest rate applicable to borrowings under such agreement will be increased by 5.0%. Under the agreement, we are required to make monthly interest-only payments through November 1, 2019 and we are required to make 24 equal monthly payments of principal, plus accrued interest, thereafter from November 1, 2019 through October 1, 2021, at which time all unpaid principal and interest becomes due and payable.

We may voluntarily prepay all, but not less than all, of the outstanding principal at any time prior to the maturity date, subject to a prepayment fee, which ranges from 0% to 2% of the outstanding principal. A final payment of $1.6 million is due upon the earlier to occur of the maturity of the loan, the acceleration or prepayment of all outstanding principal or the termination of the term loan facility.

Borrowings under the term loan facility are secured by a first priority lien on all of our assets, excluding our intellectual property. We have agreed to a negative pledge on our intellectual property and to grant a security interest on our interest in our licenses from Penn if Penn consents to such security interest. The term loan facility contains customary events of default and affirmative and negative covenants, including restrictions on our ability to pay dividends and incur additional debt, but does not contain any financial covenants.

In connection with our entry into the term loan facility, in October 2017 we issued to Silicon Valley Bank a warrant to purchase 14,064 shares of our common stock, with an exercise price per share of $5.484. The warrant has a ten-year term and includes a put option pursuant to which, in the event of an acquisition, change in control or dissolution or winding up of our company, or the expiration of the warrant, Silicon Valley Bank may require us to repurchase the warrant for a total aggregate purchase price of $250,000.

On October 19, 2017, we issued and sold an unsecured promissory note in the principal amount of $7.0 million to an affiliate of one of our stockholders. The note bears interest at a rate per annum of 8.0% and is due and payable quarterly in arrears on the 19th day of each April, July, October and January beginning on January 19, 2018. The note has a maturity date of October 19, 2022. The promissory note is contractually subordinated to the term loan facility with Silicon Valley Bank. We would be required to obtain the consent of the holder of our promissory note to increase or extend the maturity of the term loan facility with Silicon Valley Bank.

In connection with the issuance and sale of the $7.0 million promissory note, we issued to the affiliate of one of our stockholders a warrant to purchase 93,764 shares of our common stock at a price per share of $5.484, which was exercised in October 2017 prior to the IPO. The warrant was exercisable at any time but would have expired if unexercised by the closing date of our IPO. We recorded the fair value of the warrant in the aggregate amount of $430,160 as a discount to the promissory note. This amount is being accreted as additional interest expense over the term of the promissory note.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2015, 2016 and 2017:

	Year Ended December 31,		
	2015	2016	2017
Net cash used in operating activities	$ (18,855,947)	$ (26,003,078)	$ (46,595,073)
Net cash used in investing activities	—	—	—
Net cash provided by financing activities	41,236,498	14,863,020	197,375,114
Net increase (decrease) in cash and cash equivalents	$ 22,380,551	$ (11,140,058)	$ 150,780,041

Net Cash Used in Operating Activities

Net cash used in operating activities was $46.6 million for the year ended December 31, 2017 and consisted primarily of a net loss of $51.0 million adjusted for non-cash items of $5.6 million, including share-based compensation expense of $5.4 million, and a net increase in operating assets of $1.2 million, which resulted primarily from an increase in prepaid expenses of $3.9 million, offset by an increase in accrued expenses of $1.8 million and an increase in accounts payable of $0.9 million.

Net cash used in operating activities was $26.0 million for the year ended December 31, 2016 and consisted primarily of a net loss of $27.1 million adjusted for non-cash items, including share-based compensation expense of $1.1 million, and a net increase in operating assets of $0.1 million, which resulted primarily from an increase in accounts payable and accrued expenses of $0.4 million and a decrease in refundable research and development credit of $0.4 million partially offset by a decrease in refundable research and development credit of $0.4 million and a net increase in prepaid expenses and other assets of $0.8 million.

Net cash used in operating activities was $18.9 million for the year ended December 31, 2015, and consisted primarily of a net loss of $46.5 million adjusted for non-cash items, including the cost of acquired in process research and development of $26.5 million, share-based compensation expense of $0.5 million, and a net increase in operating assets of $0.6 million, which resulted primarily from an increase in accounts payable and accrued expenses of $2.1 million partially offset by an increase in refundable research and development credit of $1.3 million and an increase in prepaid expenses and other assets of $0.2 million.

Net Cash Used in Investing Activities

There was no cash used in investing activities during the years ended December 31, 2015, 2016 and 2017.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $197.4 million during the year ended December 31, 2017, compared to $14.9 million during the year ended December 31, 2016. The net cash provided by financing activities during the year ended December 31, 2017 consisted primarily of the net proceeds of $137.2 million from the issuance and sale of 10,714,000 shares of our common stock in November 2017 in our IPO as well as net proceeds of approximately $12.8 million from the issuance and sale of an additional 981,107 shares of our common stock pursuant to the underwriter's partial exercise of their over-allotment option after the IPO, and net proceeds of $19.7 million from the issuance and sale of 7,792,035 shares of series E convertible preferred stock in August 2017. In October 2017, we borrowed $20.0 million under the term loan facility with Silicon Valley Bank and issued and sold a promissory note in an original principal amount of $7.0 million to an affiliate of one of our stockholders. In October 2017, we received $0.5 million from the exercise of a warrant associated with the $7.0 million promissory note.

The net cash provided by financing activities for the year ended December 31, 2016 consisted of net proceeds of $14.9 million from the sale and issuance of 6,714,413 shares of series D convertible preferred stock in January 2016 at a per share price of $2.234.

Net cash provided by financing activities was $41.2 million during the year ended December 31, 2015. The net cash provided by financing activities for the year ended December 31, 2015 consisted of net proceeds from the sale and issuance of an aggregate of 6,183,333 shares of series C convertible preferred stock in January, March and May 2015 at a per share price of $1.50 and the issuance of 14,384,938 shares of series D convertible preferred stock in December 2015 at a per share price of $2.234.

Funding Requirements

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

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents as of December 31, 2017, will enable us to fund our operating expenses and capital expenditure requirements at least into the third quarter of 2019. We have based this estimate on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. We do not expect that the net proceeds from this offering and our existing cash and cash equivalents at December 31, 2017, will be sufficient to enable us to complete our planned Phase 3 clinical trials of APL-2 or to complete the development of APL-2 or any of our other product candidates. Because of the numerous risks and uncertainties associated with the development of APL-2 and other potential product candidates, and because the extent to which we may enter into collaborations with third parties for the development of these product candidates is unknown, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our future funding requirements will depend on many factors, including:

- the scope, progress, timing, costs and results of clinical trials of, and research and preclinical development efforts for, APL-2 and future product candidates;

- our ability to identify a collaborator for any of our product candidates and the terms and timing of any collaboration agreement that we may establish for the development and any commercialization of such product candidates;
- the number and characteristics of future product candidates that we pursue and their development requirements;
- the outcome, timing and costs of clinical trials and of seeking regulatory approvals;
- the costs of commercialization activities for any of our product candidates that receive marketing approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- subject to receipt of marketing approval, revenue, if any, received from commercial sales of our current and future product candidates;
- our headcount growth and associated costs as we expand our research and development and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims;
- the effect of competing technological and market developments;
- our ability to obtain adequate reimbursement for any product we commercialize; and
- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of medicines that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We currently do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. Debt financing, if available, would result in fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business.

If we raise funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations

The following table summarizes our significant contractual obligations as of payment due date by period at December 31, 2017:

	Payments Due by Period				
	Total	Less than 1 Year	1-3 Years	3-5 Years	More than 5 Years
Long-Term Debt	$27,000,000	$ —	$11,666,667	$15,333,333	$ —
Operating Leases(1)	1,246,550	390,344	486,348	369,858	—
Total	$28,246,550	$390,344	$12,153,015	$ 15,703,191	$ —

(1) Represents future minimum lease payments under our non-cancelable operating leases. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

We are party to two license agreements with Penn under which we license specified intellectual property from Penn. The patent rights licensed to us by Penn include patents with claims that recite a class of compounds generically covering APL-2. Each license agreement requires us to pay ongoing annual maintenance payments of $100,000 per year until the first commercial sale of a licensed product. With respect to the license for the nonophthalmic field of use, we have agreed to make milestone payments to Penn aggregating up to $1.7 million based on achieving specified development and regulatory approval milestones, and up to $2.5 million based on achieving specified annual sales milestones with respect to each of the first two licensed products. With respect to the license for the ophthalmic field of use, we have agreed to make milestone payments to Penn aggregating up to $3.2 million based on achieving specified development and regulatory milestones, and up to $5.0 million based on achieving specified annual sales milestones. The license agreements also require that we pay low single-digit royalties to Penn based on net sales of each licensed product by us and our affiliates and sublicensees and specified minimum quarterly royalty thresholds. In addition, we are obligated to pay Penn a specified portion of income we receive from sublicensees. We have not included any of these potential payments in the contractual obligations table above, as we cannot reasonably estimate whether, when and in what amount any of such payments shall be made.

We enter into agreements in the normal course of business with CROs for clinical trials and clinical supply manufacturing and with vendors for preclinical research studies and other services and products for operating purposes. We have not included these payments in the table of contractual obligations above since the contracts are cancelable at any time by us, generally upon 30 days prior written notice to the CRO, and therefore we believe that our non-cancelable obligations under these agreements are not material. Under these agreements, as of December 31, 2017, we are obligated to pay up to $1,713,000 to these vendors.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. As of December 31, 2017, we had cash and cash equivalents of $175.6 million, consisting primarily of money market funds. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our investment portfolio. We have the ability to hold our marketable securities until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments.

As of December 31, 2017, we had no liabilities denominated in foreign currencies.

BUSINESS

Overview

We are a clinical-stage biopharmaceutical company focused on the development of novel therapeutic compounds to treat disease through the inhibition of the complement system, which is an integral component of the immune system, at the level of C3, the central protein in the complement cascade. We believe that this approach can result in broad inhibition of the principal pathways of the complement system and has the potential to effectively control a broad array of complement-dependent autoimmune and inflammatory diseases.

We have the most advanced clinical program targeting C3. We believe that our lead product candidate, APL-2, has the potential to be a best-in-class treatment that may address the limitations of existing treatment options or provide a treatment option where there currently is none. APL-2 has already shown activity that we believe is clinically meaningful in clinical trials for two distinct medical conditions—geographic atrophy in age-related macular degeneration, or GA, and paroxysmal nocturnal hemoglobinuria, or PNH—and we plan to conduct clinical trials in additional complement-dependent diseases. In our Phase 2 clinical trial of APL-2 in patients with GA, treatment with APL-2 resulted in a significant reduction in the rate of GA lesion growth over 12 months, and we are planning to initiate a Phase 3 clinical program evaluating APL-2 in patients with GA. In our two ongoing Phase 1b clinical trials in PNH, APL-2 achieved improvements in transfusion dependency, hemoglobin levels and other hematological indicators that we believe are clinically meaningful. We are also developing other novel compounds targeting C3. We hold worldwide commercialization rights to APL-2 and these other novel compounds targeting C3.

In GA, we are developing APL-2 to be injected intravitreally as a monotherapy. GA is an advanced form of age-related macular degeneration, or AMD, which is a disorder of the central portion of the retina characterized by progressive retinal cell death that ultimately leads to blindness. GA is a disease with significant unmet need that affects approximately one million patients in the United States and for which there are no U.S. Food and Drug Administration, or FDA, approved therapies. In August 2017, we completed the primary endpoint analysis for the 12-month treatment period in our Phase 2 clinical trial in 246 patients, with GA and in February 2018 we completed our analysis of the results for the six-month period following the 12-month treatment period during which patients were monitored and did not receive APL-2.

In the Phase 2 trial, APL-2 achieved the primary endpoint of reduction in the rate of GA lesion growth at 12 months. Patients treated monthly with APL-2 showed a 29% reduction in the rate of GA lesion growth compared to sham, with a p-value of 0.008, and patients treated with APL-2 every other month showed a 20% reduction, with a p-value of 0.067. P-value is a conventional statistical method for measuring the statistical significance of clinical results. In our Phase 2 trial, we set statistical significance as a p-value of 0.1 or less, meaning that there is a 1-in-10 or less statistical probability that the observed results occurred by chance rather than as a result of a treatment effect. Because the p-value of these results was less than 0.1, they are statistically significant.

Additionally, in a *post hoc* analysis of the Phase 2 trial, a greater effect was observed during the second six months of the treatment period compared to the first six months. During the second six months, we observed a reduction in the rate of GA lesion growth for patients for whom images were available at six and 12 months of 47% with monthly administration compared to sham, with a p-value of less than 0.001, and a reduction of 33% with administration every other month compared to sham, with a p-value of 0.01. These results are also statistically significant.

After the 12-month treatment period, patients were monitored for a further six months without treatment. During this monitoring period, the GA lesions in the previously treated groups grew at a rate similar to sham. Patients who received monthly APL-2, and for whom images were available at 12 and 18 months, showed only a 12% reduction in the growth rate of lesions over the six-month monitoring period compared to sham, while patients who received every other month administration of APL-2 showed a 9% reduction in the growth rate compared to sham. These differences are not considered to be statistically significant.

The most frequently reported adverse events in the trial were associated with the injection procedure and are common for intravitreal injections. In addition, during the 12-month treatment period and the six-month monitoring period (18 months total), we observed a higher incidence of new onset exudation, or fluid leakage in the retinas of eyes in which exudation had not previously been observed, in the study eyes treated with APL-2 as compared to sham, predominantly in patients with a history of wet AMD in the non-study eye, or fellow eye. Specifically, we observed that, after the 12-month treatment period and the six-month monitoring period, 21% of patients who received administration of APL-2 every month and 9% of patients who received administration of APL-2 every other month showed new onset exudation in the study eye, as compared to 1% in the sham group. We submitted a safety report to the FDA in April 2017 regarding these events, and the FDA has not communicated any concern or requested additional information with regards to these findings. Patients who experienced new onset exudation in the study eye were discontinued from treatment with APL-2 and were treated with standard-of-care therapies that inhibit vascular endothelial growth factor, or VEGF, a naturally occurring protein in the body that causes the growth of abnormal blood vessels and leakage in the eye. There was no meaningful negative impact on visual acuity resulting from the new onset exudations.

Following discussions with the FDA and the EMA, we have finalized the trial design for a Phase 3 clinical program to evaluate APL-2 for the treatment of GA. The Phase 3 program, which we plan to begin in the second half of 2018, will consist of two identical 600-patient prospective, multicenter, randomized, double-masked, sham-injection controlled clinical trials to assess the efficacy and safety of multiple intravitreal injections of APL-2 in patients with GA. The Phase 3 clinical trials will be similar in design to the Phase 2 trial, including the eligibility criteria and primary endpoint of GA lesion growth, except that patients will be treated with APL-2 for 24 months in the Phase 3 trials and there will not be a monitoring period. Additionally, unlike the Phase 2 trial, patients who develop new onset exudation in the study eye will continue to be treated with APL-2 along with VEGF injections, the current standard of care for wet AMD.

We also plan to initiate a Phase 1b/2, multi-center, open label clinical trial to evaluate the safety of intravitreal APL-2 therapy when administered in parallel with anti-VEGF treatments in patients with wet AMD in the study eye in the second quarter of 2018. In this trial, we will evaluate whether treatment with APL-2 may allow wet AMD patients to reduce their dependence on anti-VEGF treatments. We believe that the data from this trial may support the use of APL-2 in eyes afflicted with both wet AMD and GA.

In PNH, we are developing APL-2 to be injected subcutaneously as a monotherapy. PNH is a rare, life-threatening, chronic, debilitating blood disorder characterized by the absence of certain proteins that normally regulate complement activity on the surface of blood cells. As a consequence, patients with PNH suffer from significant and chronic red blood cell loss, or hemolysis. The only therapy currently approved for the treatment of PNH, eculizumab (Soliris), inhibits the complement system by targeting C5, a protein that is downstream from C3 in the complement cascade. Inhibitors that target C5 are limited to addressing only one of the two mechanisms of hemolysis in PNH. Consequently, many patients with PNH who are on treatment with eculizumab remain anemic and continue to require frequent transfusions, conditions associated with a poor quality of life. By contrast, APL-2, because it targets C3, addresses both mechanisms of hemolysis and, we believe, may therefore significantly ameliorate these conditions.

In our ongoing Phase 1b trials of APL-2 for the treatment of PNH, treatment with APL-2 has been associated with improvements in transfusion dependency, levels of hemoglobin—the protein that carries oxygen from the lungs to the tissues of the body—and other hematological indicators that we believe are clinically meaningful. We made these observations both in patients who had not been treated with eculizumab, who we refer to as treatment-naïve patients, and in patients being treated with eculizumab who remained anemic and required frequent blood transfusions. In these trials, APL-2 has been generally well tolerated.

As of February 28, 2018, four of the six patients who had been treated with daily doses of 270 mg of APL-2 and with eculizumab remain on treatment in the trial, having received treatment with APL-2 for a total of between 16 and 19 months. Due to the response observed with the APL-2 treatment for each of the four

remaining patients, the treating physicians have individually taken the decision either to reduce the dose of eculizumab to the label dose for patients who had received a higher dose of eculizumab or to withdraw eculizumab treatment. We intend to report additional data from these patients in the second quarter of 2018.

Additionally, we initiated enrollment of additional treatment-naive patients in our Phase 1b clinical trial in the first quarter of 2018. In April 2018, we reported interim results as of April 13, 2018 from eight treatment-naive patients in the trial who had completed the initial 28-day treatment period with a daily dose of 270 mg of APL-2. The reported patients had a mean lactate dehydrogenase, or LDH, of 11.6 times the upper limit of normal at baseline which was reduced to a mean LDH of 0.9 times the upper limit of normal at day 28. In addition, seven of the eight patients were below the upper limit of normal at day 28. These reported patients had an average increase in hemoglobin of 4.3 g/dL from a baseline average of 7.9 g/dL to an average last measurement of 12.2 g/dL within the first 12 weeks of the treatment period. Except for two patients, each of whom received a single transfusion within the first two weeks of treatment with APL-2, no other transfusions have been reported in the trial for any patients during the treatment period. APL-2 has generally been well tolerated in the reported patients. We plan to continue enrolling treatment-naive patients in this trial and plan to report additional data in June 2018.

We plan to initiate a Phase 3 clinical trial in patients with PNH comparing treatment with APL-2 to treatment with eculizumab as a monotherapy in the second half of 2018. We plan to enroll up to 70 patients with PNH in this trial who are then receiving eculizumab. The treatment period of the trial will consist of three parts: a four-week run-in period, a 16-week randomized treatment period and a 32-week open-label APL-2 only period. During the run-in period, all patients will receive twice-weekly subcutaneous doses of 1,080 mg of APL-2 in addition to patients' then current dose of eculizumab. The run-in period is designed to provide patients with sufficient plasma concentration of APL-2 to provide for what we expect to be adequate complement inhibition before withdrawing eculizumab. Following completion of the run-in period, patients will receive either 1,080mg of APL-2 twice per week or their current dose of eculizumab through the duration of the 16-week randomized treatment period. We expect that the primary endpoint will be the week 16 change from baseline in hemoglobin level. Following completion of the randomized treatment period, all patients will receive APL-2 only for 32 weeks in the open-label part.

We are currently discussing with the FDA, the European Medicines Agency, or EMA, and the Japanese Pharmaceuticals and Medical Devices Agency, or PMDA, the trial program that we will need to conduct to submit APL-2 for regulatory approval for PNH.

In April 2014, we received orphan drug designation from the FDA for APL-2 for PNH, and in December 2016 we received fast track designation from the FDA for APL-2 for PNH. If our clinical development of APL-2 for PNH is successful, we believe that APL-2 could be a best-in-class therapy for PNH, differentiated by mechanism, and has the potential to significantly increase the quality of life of patients with PNH as compared to the current standard of care.

We plan to initiate Phase 2 clinical trials of APL-2 in patients with autoimmune hemolytic anemia, or AIHA, in the first half of 2018, and in patients with complement-dependent kidney diseases, or nephropathies, in the first half of 2018. We plan to report data from the patients with AIHA in the second quarter of 2018 and from the patients with complement-dependent nephropathies in the second half of 2018.

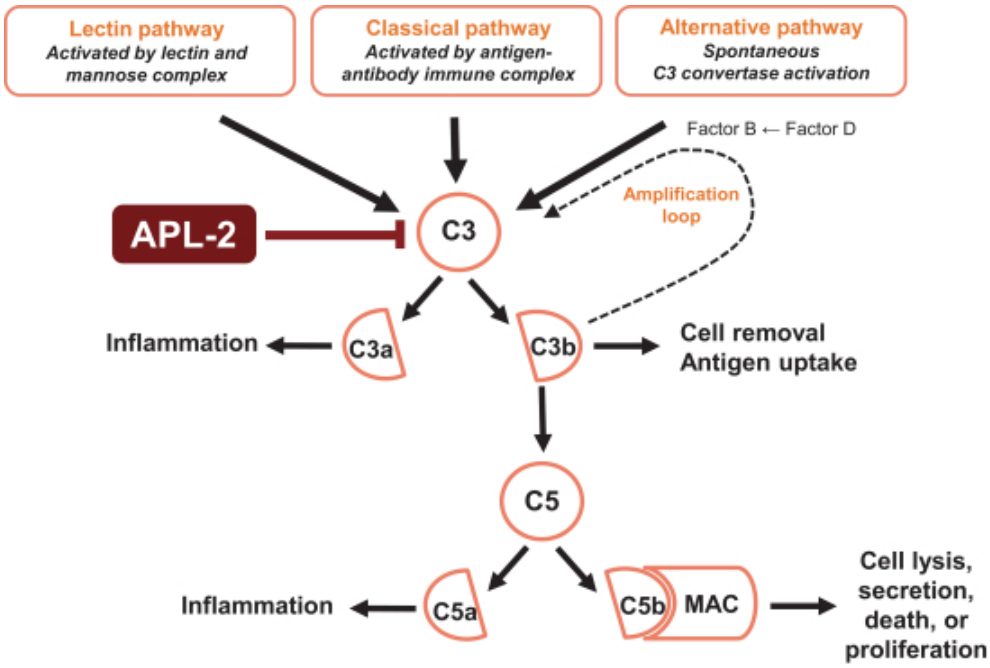
By combining our core expertise in complement inhibition with our deep understanding of complement immunology, we intend to expand our pipeline of potential treatment areas with APL-2 and with additional new product candidates, including APL-9, which we are developing for intravenous administration in systemic indications.

Our Approach

The complement system plays a pivotal role in both innate and adaptive immune systems. Complement proteins are produced primarily by the liver and circulate in the blood and through the body's tissues. The

complement system may be activated through three principal pathways, known as the classical, lectin and alternative pathways, each of which requires the C3 protein to enable three principal immune responses: opsonization, inflammation and formation of the membrane attack complex, or MAC. When C3 is activated, C3 fragments, such as C3b, tag cell surfaces in a process called opsonization, which marks the cells for removal from tissues or the bloodstream. Two other fragments, C3a and C5a, are released, contributing to inflammation in the surrounding tissues. Further complement activation causes membrane attack complex formation on cell surfaces, piercing holes and causing cells to lyse, or rupture.

The following figure depicts the complement system, its three principal activation pathways and its principal effects:



Under conditions of excessive or uncontrolled activation, the complement system is believed to play a key role in the incidence and progression of several autoimmune and inflammatory diseases. In these diseases, the complement system acts directly through tissue destruction by the membrane attack complex and indirectly by signaling other elements of the immune system to inappropriately target otherwise healthy tissues. Because the contribution of complement activation to the development and progression of these diseases is not fully understood, it has been difficult to develop therapeutics that ameliorate the conditions contributing to these diseases by targeting only one of the complement activation pathways.

Complement activation and its effects can be inhibited in multiple ways. By targeting complement proteins upstream of C3, one of the three principal activation pathways can be inhibited. For example, inhibition of factor D results in inhibition of the alternative pathway, but not the classical or lectin pathways. The complement system can also be inhibited by targeting complement proteins downstream of C3, which results in limited inhibition of complement effects. For example, inhibition of C5 leads to inhibition of the formation of the membrane attack complex and C5a-mediated inflammation, but does not affect opsonization or C3a-mediated inflammation.

We have designed APL-2 to target complement proteins centrally at the level of C3. We believe that this approach can result in broad inhibition of the complement pathways and has the potential to effectively control

complement-dependent diseases, including GA, PNH, AIHA and complement-dependent nephropathies. We believe that APL-2 has the potential to be a best-in-class treatment and may address the limitations of existing treatment options or provide a treatment option where there is none.

We also believe that APL-2 may act as an immunotherapy, which refers to the clinical regulation of an overly permissive or overly aggressive immune system for therapeutic purposes. In the field of oncology, innovative approaches to immunotherapy have been used to correct an overly permissive immune system that fails to properly eliminate cancer cells. These approaches have led to unprecedented rates of prolonged disease-free survival in certain cancers. In autoimmune disease, we believe immunotherapy may be used to correct an overly aggressive immune system. We further believe that C3 inhibition has the potential to correct the immunological dysfunction that underlies multiple autoimmune and inflammatory diseases by enabling the natural regulatory mechanisms of immunity to normalize the immune response. We refer to this corrective approach as complement immunotherapy. As with cancer, we believe that the next breakthrough treatments in autoimmune disease may stem from novel approaches to immunotherapy, such as complement immunotherapy.

Strategy

We aim to become a leading biopharmaceutical company focused on the discovery, development and commercialization of therapeutics to treat autoimmune and inflammatory diseases through complement inhibition. To achieve this goal, we are pursuing the following strategies:

- ***Advance APL-2 (intravitreal administration) into Phase 3 clinical development in GA and Phase 1b/2 clinical development in wet AMD***. We are developing APL-2 as monotherapy for GA, administered by intravitreal injections. In our Phase 2 clinical trial of APL-2 in patients with GA, treatment with APL-2 resulted in a significant reduction in the rate of GA lesion growth at 12 months compared to sham. We plan to initiate Phase 3 clinical trials of APL-2 in GA in the second half of 2018 and to initiate a Phase 1b/2 trial of APL-2 in patients with wet AMD in the second quarter of 2018.
- ***Advance APL-2 (systemic administration) into Phase 3 clinical development in PNH.*** We are developing APL-2 as monotherapy for patients with PNH, administered by subcutaneous injection. In our ongoing Phase 1b clinical trials of APL-2 in patients being treated with eculizumab and in treatment-naïve patients, APL-2 treatment was associated with improvements in transfusion dependency, hemoglobin levels and other hematological indicators that we believe are clinically meaningful. We plan to initiate a Phase 3 clinical trial in patients with PNH in the second half of 2018.
- ***Expand APL-2 (systemic administration) into new indications with demonstrated complement involvement.*** Complement has been found to be implicated in multiple diseases. We believe that APL-2 has the potential to be an effective treatment for patients with these diseases. We plan to initiate a Phase 2 clinical trial of APL-2 in AIHA in the first half of 2018 and a Phase 2 clinical trial of APL-2 in complement-dependent nephropathies in the first half of 2018.
- ***Expand our pipeline by developing new compounds and programs for other complement-dependent diseases***. By combining our core expertise in complement inhibition with our understanding of immunology and the role of the complement system in disease, we believe that we are well positioned to continue to develop a pipeline of treatments for a broad range of autoimmune and inflammatory diseases. We are developing new product candidates for the treatment of complement-dependent diseases, including APL-9, which we are developing for intravenous administration in systemic indications.
- ***Develop a custom drug delivery system for systemic administration of APL-2***. We are developing a custom, on-body drug delivery system that would enable patients to self-administer APL-2 through subcutaneous infusion more easily than with currently available off-the-shelf, FDA-approved or FDA-cleared devices. While our goal is to commercially launch APL-2 in PNH together with the drug delivery system, we can commercialize APL-2 without the custom drug delivery system, in which case marketing approval for APL-2 will not be contingent upon approval of the drug delivery system.

- ***Prepare for commercialization of APL-2***. We hold worldwide commercialization rights to APL-2 and our other product candidates. As a result, we have the flexibility to develop and potentially commercialize products ourselves, or alternatively to seek to enter into collaborations with industry partners.

Our Programs

Our lead product candidate, APL-2, is a C3 inhibitor. APL-2 is a conjugate of a compstatin analogue, formulated both for intravitreal injection, which is an injection directly into the eye, and systemic administration by subcutaneous injection, which is an injection into the tissue under the skin.

The following table summarizes key information about our clinical program for APL-2:

Indication	Clinical Trials	Trial Participants	Estimated Timeline
Ophthalmology *(intravitreal)*			
GA	Phase 1 single ascending dose trial	Patients with wet AMD	Completed
	Phase 2 trial	Patients with GA	Completed
	Planned Phase 3 trials	Patients with GA	Initiate 2H 2018
Wet AMD	Planned Phase 1b/2 trial	Patients with wet AMD	Initiate 2Q 2018
Hematology *(systemic)*			
PNH	Phase 1 single ascending dose trial	Healthy volunteers	Completed
	Phase 1 multiple ascending dose trial	Healthy volunteers	Completed
	Phase 1b trial	Eculizumab-treated patients with PNH	Additional data 2Q 2018
	Phase 1b trial	Treatment-naïve patients with PNH	Additional data 2Q 2018
	Planned Phase 3 trial	Patients with PNH	Initiate 2H 2018
AIHA	Planned Phase 2 trial	Patients with AIHA	Initiate 1H 2018; data 2Q 2018
Nephrology *(systemic)*			
Complement-dependent Nephropathies	Planned Phase 2 trial	Patients with complement-dependent nephropathies	Initiate 1H 2018; data 2H 2018

Ophthalmology (intravitreal APL-2)

Geographic Atrophy

Background

GA is a type of advanced age-related macular degeneration, or AMD. AMD is a disorder of the central portion of the retina in the eye, known as the macula, which is responsible for central vision and color perception. AMD affects vision in one or both eyes and results in progressive and chronic degeneration of the macula, often resulting in irreversible vision loss. AMD is a disease of aging, typically occurring after the age of 50. In the early stage of the disease, yellow deposits, or drusen, appear under the retina. Over time, the disease can progress to an intermediate stage where drusen deposits grow larger and other changes reflective of disease progression appear. Patients with intermediate AMD are at risk of progressing to GA or wet AMD. In contrast to intermediate AMD, these advanced forms are associated with progressive and often severe vision loss. GA is characterized by a degenerative process resulting in the progressive loss of retinal cells, which over the course of several years results in blindness.

Wet AMD is characterized by the rapid abnormal growth of blood vessels beneath the retina and leakage. If left untreated, wet AMD rapidly progresses to severe vision loss. Wet AMD is typically treated with anti-VEGF therapies. Some wet AMD patients require only a few anti-VEGF injections to resolve the condition and do not require further treatment. These patients have good long-term visual outcomes. Other patients become dependent on chronic and repetitive anti-VEGF injections. In a third-party study of wet AMD patients in clinical trials of an anti-VEGF therapy, known as the SEVEN-UP study, 98% of patients dependent on chronic and repetitive anti-VEGF injections developed GA within seven years and GA affected central vision in 90% of these patients. Based on the SEVEN-UP study, we believe that patients with wet AMD who receive chronic anti-VEGF treatments may suffer from significant long-term vision loss as the result of the development of GA.

According to the Brightfocus Foundation, over ten million people in the United States have some form of AMD. Based on published studies, we believe that at least one million people in the United States have GA.

The mechanism by which complement activation is upregulated and can damage the retina is poorly understood. However, we believe that the upregulation of complement activation due to immune dysregulation damages retinal cells in two ways. First, retinal cells are damaged by inflammation caused by increased levels of C3a and C5a. Second, the increased deposition of C3b on the cell surface of retinal cells caused by complement activation, combined with the limited ability of cells to remove C3 activated fragments such as C3b, leads to the accumulation of C3 fragments on the retinal cells. The presence of C3a and C5a, as well as C3 fragment deposition on retinal cells, activates macrophages and microglia. Macrophages are large white blood cells that form part of the immune system that engulf and digest cells, debris and foreign substances. Macrophages also play an important role in modulating other parts of the immune system. Microglia are a type of tissue-residing macrophage located in the brain, spinal cord and retina.

Because APL-2 both blocks the production of C3a and C5a and prevents the accumulation of C3 fragments on retinal cells through the inhibition of C3, we believe that APL-2 may allow the retinal environment to return to its quiescent state. We do not believe that selective inhibitors of the alternative pathway, such as lampalizumab, a complement factor D inhibitor, which only partially blocks the formation of C3b on the retinal cell surface, or C5 inhibitors, which cannot prevent C3b deposition on retinal cells, can cause the retinal environment to return to its quiescent state.

Current Therapies and Their Limitations

There are no therapies approved to treat GA. There are, however, other therapies in development for GA. Zimura, a C5 inhibitor being developed by Ophthotech Corporation, is in Phase 2/3 clinical trials. Lampalizumab, which had been developed by F.Hoffmann-La Roche AG, or Roche, failed to meet its primary endpoint in its Phase 3 clinical trials.

Benefits of Our Approach

We believe APL-2, with its inhibition of complement activation at the level of C3, may provide the following benefits:

- *Prevention or reduction of the rate of retinal cell death progression*. We believe APL-2 may mitigate or prevent retinal cell death in GA. In our Phase 2 trial of APL-2 in patients with GA, treatment with APL-2 resulted in a significant reduction in the rate of GA lesion growth over 12 months.
- *Potential application to all patients with GA independent of complement pathway causing disease progression.* APL-2, by targeting C3, has been designed to inhibit all three principal complement activation pathways and may therefore be effective in a broad patient population. We believe, based on the genetic marker and other data from our analysis of the Phase 2 trial that the activity of APL-2 may not be dependent upon the activation of any particular complement pathway.

- *Potential for every other month administration*. In our Phase 2 clinical trial of APL-2 in GA, APL-2 met its primary endpoint in both the monthly and the every other month APL-2 administration treatment arms.

Clinical Development

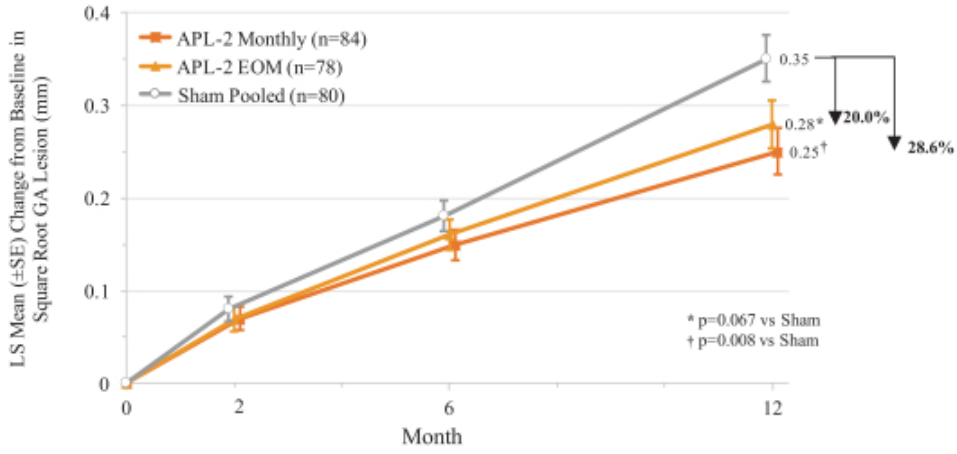
We conducted a Phase 2 clinical trial of APL-2 in patients with GA. In August 2017, we completed the primary endpoint analysis for the 12-month treatment period in that trial and in February 2018 we completed the analysis of data from the six-month monitoring period. Prior to the GA trial, we completed a Phase 1 clinical trial of APL-2 in patients with wet AMD in 2016. In November 2014, we submitted an investigational new drug application, or IND, to the FDA for the clinical development of APL-2 for the treatment of GA.

Phase 2 Clinical Trial in GA

In the third quarter of 2015, we initiated a Phase 2 multicenter, randomized, single-masked, sham-controlled clinical trial of APL-2 in patients with GA at more than 40 clinical sites, primarily located in the United States. We enrolled 246 patients in the trial. Patients were randomized in a 2:2:1:1 manner to receive APL-2 monthly, APL-2 every other month, sham injection monthly or sham injection every other month. Patients in the APL-2 arms received a dose of 15 mg of APL-2 injected intravitreally in a 0.1 cc volume, monthly or every other month for 12 months followed by six months of monitoring without treatment. In the sham-injection cohorts, patients receive a simulated injection. Study eyes received up to 13 injections in the monthly arm, and up to seven injections in the every other month arm. Eyes were evaluated for GA at the end of months two, six and 12 and will be evaluated at the end of month 18, in each case using fundus autofluorescence photographs. Fundus autofluorescence photographs are a standard imaging format used by ophthalmologists to measure and quantify clinical features of geographic atrophy.

We conducted this trial to assess the safety, tolerability, pharmacokinetics, or PK, and evidence of activity of multiple intravitreal injections of APL-2 in patients with GA in at least one eye. The primary efficacy endpoint was change in the square root of GA lesion size from baseline to month 12 in each treatment arm when compared to sham in the modified intent to treat population, which included 84 patients receiving administration of APL-2 every month, 78 patients receiving administration of APL-2 every other month and 80 patients in the group receiving sham injections. The primary safety endpoint was the number and severity of local and systemic treatment emergent adverse events. The trial was monitored by a safety monitoring committee.

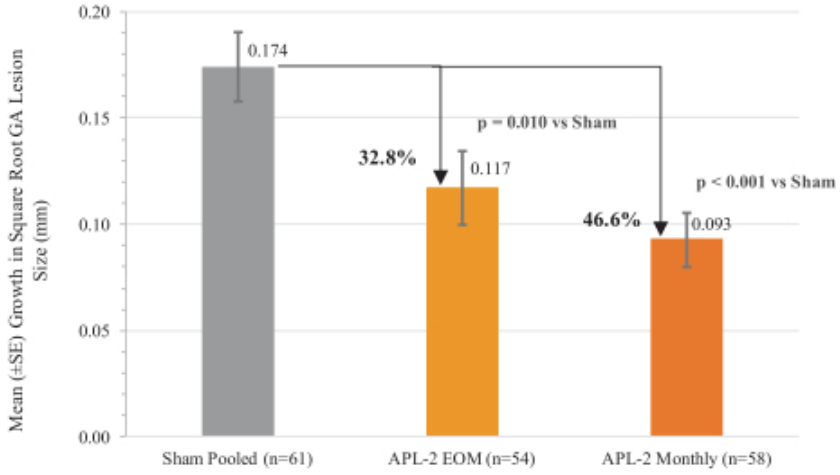
Efficacy Analysis. We announced 12-month results of the Phase 2 trial in August 2017. After 12 months, patients treated monthly with APL-2 showed a 29% reduction in the rate of GA lesion growth compared to sham, with a p-value of 0.008, and patients treated every other month showed a 20% reduction compared to sham, with a p-value of 0.067. The rate of GA lesion growth in the sham was consistent with the rate of lesion growth in patients with GA in third-party historical studies. These data are shown in the figure below.



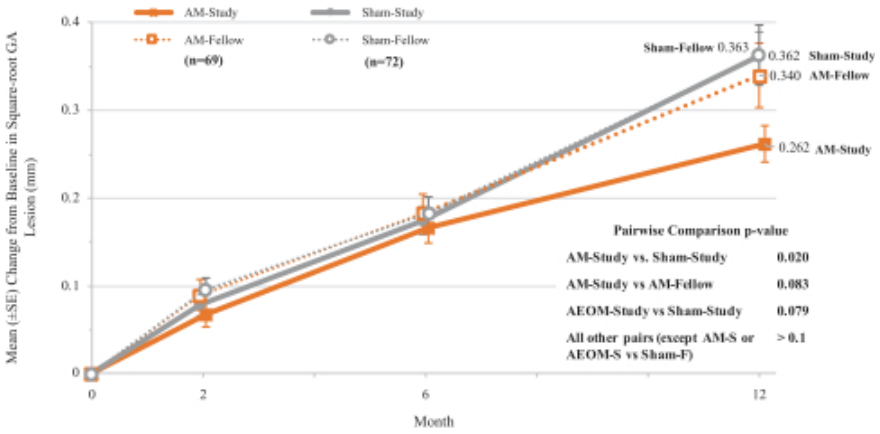
EOM = Every other month

We set statistical significance as a p-value of 0.1 or less, meaning that there is a 1-in-10 or less statistical probability that the observed results occurred by chance rather than as a result of a treatment effect. Because the p-value of these results was less than 0.1, they are statistically significant.

Additionally, in a *post hoc* analysis of the Phase 2 clinical trial, a greater effect was observed during the second six months of the treatment period compared to the first six months. During the second six months, we observed a reduction in the rate of GA lesion growth of 47% with monthly administration compared to sham, with a p-value less than 0.001, and a reduction of 33% with administration every other month compared to sham, with a p-value of 0.01. These results are also statistically significant. This *post hoc* analysis, shown in the figure below, was conducted in fewer patients than were included in the primary endpoint analysis because only patients with images available at both six and 12 months could be analyzed *post hoc*.



The activity of APL-2 was also shown in a *post hoc* analysis of the impact of APL-2 on patients with GA in both the study eye and the fellow eye, or bilateral GA. A published study has shown that growth rates of GA lesion size are similar in both eyes of patients with bilateral GA. We also made this observation in patients with bilateral GA in the sham group. In the trial, patients with bilateral GA received treatment with APL-2 in one eye and did not receive treatment in the other eye. We conducted this *post hoc* analysis because a comparison of effects in both eyes of individual patients allows the treatment effect of APL-2 to be analyzed independently of potential differences in the baseline characteristics of patients in each arm of the trial. In the trial, the rate of GA lesion growth in the study eye of patients with bilateral GA receiving administration of APL-2 every month was slower than the rate of growth in their fellow eye, with a p-value of 0.083. For the patients with bilateral GA receiving administration of APL-2 every other month, the rate of GA lesion growth was also slower in the study eye than the rate of growth in their fellow eye, but with a p-value greater than 0.1. In addition, in both treatment groups the rate of GA growth in the untreated fellow eye was slower than in the sham group. These results are shown in the figure below.



AM – APL-2 monthly; AEOM – APL-2 every other month.

As part of our review of the data, we also conducted an analysis of the treatment effect as measured by the rate of GA lesion growth in patients treated with APL-2 across multiple genetic subpopulations, including complement factor I (CFI) genotypes. We did not observe any difference in treatment effect across the subpopulations.

After the 12-month treatment period, patients were monitored for a further six months without treatment. During the monitoring period, the GA lesions in the previously treated groups grew at a rate similar to sham but the treatment effect was maintained for the full 18 months. Patients for whom images were available at 12 and 18 months who received monthly APL-2 showed a 12% reduction in the growth rate of lesions over the six-month monitoring period compared to sham, while patients who received every other month administration of APL-2 showed a 9% reduction in the growth rate of lesions over the six-month monitoring period compared to sham. These differences are not considered to be statistically significant. In the modified intent to treat population over the full 18-month period, patients who received monthly APL-2 showed a 20% reduction in the growth rate of lesions over the full 18-month period compared to sham, while patients who received every other month administration of APL-2 showed a 16% reduction in the growth rate of lesions over the full 18-month period compared to sham.

Safety Analysis. The most frequently reported adverse events in the trial were associated with the injection procedure in the study eye. These adverse events included two cases of confirmed endophthalmitis and one case of presumed endophthalmitis where the culture tested negative for bacterial growth. In the latter case, the patient fully recovered visual acuity. In our Phase 2 trial, we observed an incidence rate of endophthalmitis of 0.21% per injection. We believe the incidence of endophthalmitis may be due in part to our use of a freeze-dried material requiring reconstitution prior to injection during our Phase 2 trial, which introduced an additional risk of

contamination. We intend to use a liquid instead of the freeze-dried formulation in our Phase 3 trial, which we believe may reduce the incidence of endophthalmitis.

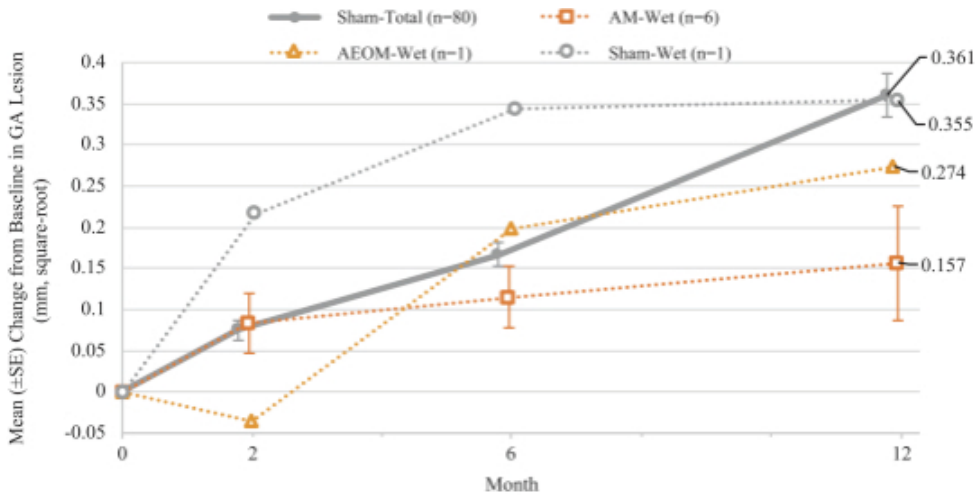
In addition, during the 12-month treatment period and the six-month monitoring period, we observed a higher incidence of new onset exudation in the study eyes treated with APL-2 as compared to sham, predominantly in patients with a history of wet AMD in the fellow eye. Specifically, we observed that, after the 12-month treatment period and the six-month monitoring period, 18 patients (21%) receiving administration of APL-2 every month and seven patients (9%) receiving administration of APL-2 every other month showed new onset exudation in the study eye, as compared to one patient (1%) in the sham group.

Patients who experienced new onset exudation in the study eye were discontinued from treatment with APL-2 and, in all but one case, treated with standard of care anti-VEGF injections under supervision. There was no meaningful negative impact on visual acuity resulting from the new onset exudations.

The development of new onset exudation by patients in the trial was communicated to the safety monitoring committee after six months of study data were available. The safety monitoring committee reviewed the cases of new onset exudation, and met several times to discuss the study data, including visual acuity, assessed the risks and benefits of continued treatment and decided that the trial should continue as planned. All mandated safety monitoring committee meetings have been held and no further safety monitoring committee meetings are scheduled.

We submitted a safety report to the FDA in April 2017 regarding these events, and the FDA has not communicated any concern or requested additional information with respect to these findings.

We observed a pronounced treatment effect in patients who experienced exudation in the study eye. In a *post hoc* analysis of the 12-month data, a subset of patients who experienced exudation in the study eye, and for whom images were available at baseline, two, six and 12 months, had pronounced reductions in the growth rate of GA lesion size as shown in the figure below. However, given the small number of patients in these groups, this observation was not statistically significant.



Note: Sample size for sham-total includes all sham patients and the sample size for all other groups includes patients who had images at baseline, two, six and 12 months.

We also observed a treatment effect in patients who did not experience exudation in their study eye. In a *post hoc* analysis, when patients who experienced exudation in the study eye were excluded from the analysis,

71 patients receiving administration of APL-2 every month showed a 28% reduction in the growth rate of GA lesion size as compared to 80 sham patients, with a p-value of 0.011, and 73 patients receiving administration of APL-2 every other month showed a 24% reduction in the growth rate of GA lesion size as compared to sham, with a p-value of 0.028.

In a *post hoc* analysis of the 12 month data, after excluding patients with wet AMD in the fellow eye, five patients (10%) receiving monthly administration of APL-2 and two patients (4%) receiving administration every other month of APL-2 experienced exudation in the study eye. In the Phase 2 trial, a total of 93 patients (36%) had wet AMD in the fellow eye at the start of the trial, and we observed that these patients were more likely to show new onset exudation in the study eye than patients without wet AMD in the fellow eye. Wet AMD was present in 27% in the fellow eye of patients with GA in a published third-party study.

Phase 1 Clinical Trial

We conducted a Phase 1 open label, ascending single-dose clinical trial of APL-2 administered by intravitreal injection in patients with wet AMD who were receiving anti-VEGF therapy. We conducted the trial at multiple clinical sites both within and outside the United States to assess safety, tolerability and PK of APL-2. In this trial, patients received a single dose of APL-2 by intravitreal injection followed by 113 days of monitoring. We originally planned to enroll nine patients in the trial, in three cohorts of three patients each, at doses of 5 mg, 10 mg and 20 mg of APL-2. In August 2015, after completing enrollment of all three cohorts, we expanded the third cohort from three to 12 patients, for a total of 18 patients in this trial.

In this trial, APL-2 was well tolerated, and no serious adverse events were reported.

Based on the results, we determined to evaluate a dose of 15 mg in our Phase 2 clinical trial.

Planned Phase 3 Clinical Trials

Following discussions with the FDA and the EMA, we have finalized the trial design for a Phase 3 clinical program to evaluate APL-2 for the treatment of GA. The Phase 3 program, which we plan to begin in the second half of 2018, will consist of two identical 600-patient prospective, multicenter, randomized, double-masked, sham-injection controlled trials to assess the efficacy and safety of multiple intravitreal injections of APL-2 in patients with GA. The Phase 3 clinical trials will be similar in design to the Phase 2 trial, including the eligibility criteria and primary endpoint of GA lesion growth , except that patients will be treated with APL-2 for 24 months in the Phase 3 trials and there will not be a monitoring period following treatment. Additionally, unlike the Phase 2 trial, GA lesion size will be measured by total area rather than mean change in the square root of GA lesion size. These measurements will be made at 12 months and 24 months. We expect that we will set statistical significance as a p-value of 0.05 or less, meaning that there is a 1 in 20 or less probability that the observed results occurred by chance. Patients who develop new onset exudation in the study eye will continue to be treated with APL-2 along with VEGF injections, the current standard of care for wet AMD.

The observation intervals in pivotal studies in AMD are typically 24 months in total duration in order to meet regulatory requirements for long-term safety and to demonstrate durability of the treatment effect on anatomical and functional endpoints. However, based on our experience in the Phase 2 trial, we believe that APL-2 can show treatment effect at 12 months and we therefore plan to analyze the data after all patients have completed 12 months of treatment in the trial in addition to the final assessment after 24 months of treatment. This design is in line with the recommendations of the FDA and the EMA.

Planned Phase 1b/2 Clinical Trial in Wet AMD

We plan to initiate a Phase 1b/2, multi-center, open label trial to evaluate the safety of intravitreal APL-2 therapy when administered in parallel with anti-VEGF treatments in patients with wet AMD in the second

quarter of 2018. In this trial, we will evaluate whether treatment with APL-2 may allow patients with wet AMD in the study eye to reduce their dependence on anti-VEGF treatments. We believe that the data from this trial may support the use of APL-2 in eyes afflicted with both wet AMD and GA.

Supporting Trial

We plan to initiate a long-term safety extension clinical trial in the second half of 2018 to support continued intravitreal dosing with APL-2 for patients with GA who have previously participated in a clinical trial with APL-2.

Preclinical Studies

We have conducted preclinical studies in monkeys to assess the safety of APL-2 injected intravitreally. A full toxicological review, including histopathological examinations of both eyes and of multiple additional tissues from each monkey revealed no evidence of APL-2-related toxicity changes at any of the doses tested.

Hematology (systemic APL-2)

Paroxysmal Nocturnal Hemoglobinuria

Background

PNH is a rare, chronic, debilitating blood disorder that is most frequently acquired in early adulthood and usually continues throughout the life of the patient. Some of the prominent symptoms of PNH include severe anemia, a condition that results from having too few red blood cells, severe abdominal pain, severe headaches, back pain, excessive weakness, fatigue and recurrent infections. If not treated, PNH results in the death of approximately 35% of affected individuals within five years of diagnosis and 50% of affected individuals within ten years of diagnosis, primarily due to the formation of life-threatening blood clots inside the blood vessels, or thrombosis. Based on prevalence data published in an abstract in a peer-reviewed journal, we estimate that there are approximately 4,700 patients with PNH in the United States.

PNH is caused by the presence of mutant stem cells in the bone marrow that lack important proteins on their surface that protect against activation of the complement system. In patients with PNH, an autoimmune response targets and eliminates normal stem cells, enabling mutant cells to become dominant in the bone marrow. These mutant stem cells lead to mutant platelets and red blood cells that, unlike normal cells, are overly susceptible to activation or destruction by the complement system. Mutant platelets, activated by the membrane attack complex, increase the risk of thrombosis, which is the leading cause of mortality in patients with PNH. Mutant red blood cells are susceptible to destruction by intravascular and extravascular hemolysis. Intravascular hemolysis, which involves the destruction of blood cells within the blood vessels, is caused by the formation of the membrane attack complex on the surface of red blood cells causing them to rupture. Intravascular hemolysis causes severe anemia and contributes to the risk of thrombosis. Extravascular hemolysis, which involves the destruction of blood cells outside the blood vessels, is caused by C3-related opsonization on red blood cells leading to removal of the cells from the blood stream by the liver and the spleen. Extravascular hemolysis further contributes to severe anemia and transfusion dependency in patients with PNH.

Current Therapies and Their Limitations

The only approved drug for the treatment of PNH is eculizumab, marketed as Soliris by Alexion Pharmaceuticals, Inc., or Alexion. Eculizumab had reported worldwide sales of more than $2.8 billion in 2016 for its two approved indications, PNH and atypical hemolytic-uremic syndrome, or aHUS. We believe the price per year for treatment with eculizumab is approximately $500,000 in adults. Eculizumab, which is administered every two weeks intravenously, or directly into the veins, is designed to treat PNH by targeting C5 and preventing the formation of the membrane attack complex and intravascular hemolysis. Many patients with PNH

on treatment with eculizumab continue to be anemic. In addition, in a third-party study, 35% to 40% of patients on eculizumab continued to be transfusion dependent for 30 months following the beginning of treatment. We believe that inability of eculizumab to control extravascular hemolysis is responsible in part for these continuing complications.

Alexion is evaluating ALXN1210, its second-generation C5 inhibitor, in Phase 3 clinical trials as a potential treatment for patients with PNH, administrated intravenously every eight weeks and subcutaneously once per week. ALXN1210 is designed to have a longer half-life and greater inhibition of C5 than eculizumab.

Benefits of Our Approach

We believe that, because APL-2 inhibits complement activation at the level of C3, APL-2 may provide the following benefits in controlling PNH:

- *Prevention of intravascular hemolysis and its consequences*. APL-2 prevents the formation of the membrane attack complex and may thereby prevent the activation of mutant platelets and intravascular hemolysis, thus reducing the risk of thrombosis, the leading cause of mortality in PNH, as well as reducing anemia.
- *Prevention of extravascular hemolysis and its consequences*. APL-2 prevents C3b opsonization, and may thereby prevent extravascular hemolysis, further reducing anemia and transfusion dependency in patients with PNH.
- *Ease and convenience of use*. We have formulated APL-2 so that it may be self-administered by patients with PNH by subcutaneous injection. Because APL-2 is stable at room temperature for weeks in liquid, patients will be able to self-administer APL-2 without a visit to the physician. We are initially developing APL-2 for self-administration, either daily or less frequently (such as twice per week). We believe that the ability to self-administer APL-2 on a regular basis could improve the quality of life for patients with PNH. We are developing a drug delivery system to facilitate APL-2's ease of use and self-administration for patients.

Clinical Development

Our clinical development program is guided by a planned commercial switch-over strategy for APL-2. Under this strategy, following marketing approval, we plan to allow PNH patients on treatment with eculizumab to assess the benefit of APL-2 in co-treatment with eculizumab for a limited time, before deciding to switch to APL-2 monotherapy or to revert to eculizumab monotherapy. We are conducting two clinical trials of APL-2 as part of our PNH program: a Phase 1b clinical trial in patients with PNH being treated with eculizumab and a Phase 1b clinical trial in treatment-naïve patients. These trials are designed to assess safety and tolerability and whether APL-2 has the potential to control PNH. In these trials, we are measuring hemoglobin levels, which are significantly lower in patients with PNH, whether or not treated with eculizumab, and blood reticulocyte count, which is an indicator of overall hemolysis (both intravascular and extravascular) in patients on eculizumab. We are also measuring intravascular hemolysis based on LDH levels, which can be ten times higher than normal in patients with PNH, bilirubin, which is a breakdown product of hemoglobin and may be higher in patients who experience hemolysis, and the clonal distributions of normal red blood cells and mutant red blood cells unprotected from the membrane attack complex.

In both Phase 1b trials to date, patients treated with APL-2 have experienced reductions in LDH levels and improved hemoglobin levels. Furthermore, we have observed lower reticulocyte counts in patients treated with APL-2, which we believe reflects that the bone marrow is producing fewer red blood cells because fewer red blood cells are destroyed by hemolytic activity. We believe that the clonal distribution of red blood cells in treated patients suggests that fewer mutant cells are destroyed by hemolytic activity.

We plan to initiate a Phase 3 clinical trial in patients with PNH comparing treatment with APL-2 to treatment with eculizumab as a monotherapy in the second half of 2018. We plan to enroll up to 70 patients with

PNH in this trial who are then receiving eculizumab. The treatment period of the trial will consist of three parts: a four-week run-in period, a 16-week randomized treatment period and a 32-week open-label APL-2 only period. During the run-in period, all patients will receive twice-weekly subcutaneous doses of 1,080 mg of APL-2 in addition to patients' then current dose of eculizumab. The run-in period is designed to provide patients with sufficient plasma concentration of APL-2 to provide for what we expect to be adequate complement inhibition before withdrawing eculizumab. Following completion of the run-in period, patients will receive either 1,080mg of APL-2 twice per week or their current dose of eculizumab through the duration of the 16-week randomized treatment period. We expect that the primary endpoint will be the week 16 change from baseline in hemoglobin level. Following completion of the randomized treatment period, all patients will receive APL-2 only for 32 weeks in the open-label part.

We are currently discussing with the FDA, the EMA, and the PMDA the trial program that we will need to conduct to submit APL-2 for regulatory approval for PNH.

In addition, we are conducting supporting trials to determine the safety, PK and pharmacodynamic, or PD, of APL-2 in healthy volunteers of Japanese descent and to determine the renal PK in healthy volunteers. We are conducting a trial in healthy volunteers to assess the PK of a less frequent dosing regimen.

In July 2014, we submitted an IND to the FDA for the clinical development of APL-2 for the treatment of PNH. In April 2014, we received orphan drug designation from the FDA for APL-2 for PNH and in December 2016 received fast track designation from the FDA for PNH.

In all trials of APL-2 administered systemically by subcutaneous injection, we have monitored the safety of our targeting of C3 closely. Individuals who lack functional levels of C3 or C5 have been shown to be susceptible to infection by certain bacterial species, including *Neisseria meningitidis* in C5-deficient individuals and *Neisseria meningitidis*, *Streptococcus pneumoniae* and *Haemophilus influenzae* in C3-deficient individuals. As a result, we vaccinate patients in these trials against these three pathogens, which we believe minimizes the risk of infection. In our clinical trials of APL-2 using subcutaneous administration, which we have conducted in more than 70 patients and healthy volunteers, we have not observed any infections of concern.

Ongoing Phase 1b Clinical Trial with Patients on Eculizumab

We are conducting a Phase 1b open-label, single and multiple ascending dose clinical trial of APL-2 in patients with PNH who are receiving eculizumab that we initiated in February 2015. We are conducting this trial at multiple clinical sites in the United States.

In this clinical trial, doses of APL-2 are administered by subcutaneous injection to patients with PNH who are concurrently being treated with eculizumab at varying doses according to the treating physicians' recommendations. We initially enrolled eight patients with PNH who participated in one of four cohorts. Each cohort was composed of two patients. The first two cohorts received a single dose of APL-2 ranging from 25 mg to 50 mg, and then, after a 28-day monitoring period, received daily doses of APL-2 for an additional 28 consecutive days at doses ranging from 5 mg/day to 30 mg/day. The other two cohorts received daily doses of 180 mg and 270 mg. Based on the combined safety and PD data from this and our other trials of APL-2, we amended the protocol to increase the number of patients in the fourth cohort to six and to provide that patients in the fourth cohort would receive a dose of 270 mg/day for up to two years.

APL-2 has been generally well tolerated by the patients in the trial with 12 serious adverse events reported across three patients. Only one of these serious adverse events was noted as possibly related to the administration of APL-2. The patient with this serious adverse event experienced liver pain and elevated liver enzyme levels. As a result, treatment with APL-2 was temporarily discontinued but treatment with eculizumab continued. This discontinuation was followed by a recurrence of anemia and required a blood transfusion. Treatment with APL-2 was reinitiated at a dose of 180 mg and then increased to 270 mg, and the patient's hemoglobin levels increased.

The patient later underwent surgery to improve the flow of bile. This intervention resulted in a lowering of the liver enzyme levels, which thereafter remained low.

The first two cohorts, in which patients received a dose of 5 mg/day or 30 mg/day of APL-2 for 28 days, did not show evidence of pharmacological activity. In the third cohort, in which patients received a dose of 180 mg/day, there were relevant changes in hematological indicators. Hemoglobin levels increased in both patients during the first two weeks of treatment and remained stable until the end of treatment on Day 28. There was also a reduction in reticulocyte counts. No patient required a red blood cell transfusion during the treatment period, in contrast to the period prior to the start of dosing.

In the fourth cohort, six patients received single doses of 270 mg/day of APL-2 for 28 days. After 28 days of treatment, all six patients experienced clinical improvement associated with relevant changes in hematological indicators and APL-2 treatment was continued. Hemoglobin levels increased and reticulocyte counts decreased in all six patients, and reached the normal range in five of the six patients. LDH levels decreased in all six patients. Additionally, C3 fragment deposition on mutant red blood cells was reduced in these patients. We have continued to monitor the patients in the fourth cohort, and during the six-month period following the 28-day monitoring period, the patients' hemoglobin levels have remained in the normal range and LDH levels have continued to decrease.

As of February 28, 2018, four of the six patients who had been treated with daily doses of 270 mg of APL-2 and with eculizumab remain on treatment in the trial, having received treatment with APL-2 for a total of between 16 and 19 months. Due to the response observed with the APL-2 treatment for each of the four remaining patients, the treating physicians have individually taken the decision either to reduce the dose of eculizumab to the label dose for patients who had received a higher dose of eculizumab or to withdraw eculizumab treatment. We intend to report additional data from these patients in the second quarter of 2018.

Ongoing Phase 1b Clinical Trial with Treatment-Naïve Patients

We are conducting a Phase 1b open-label clinical trial of APL-2 in treatment-naïve patients with PNH that we initiated in December 2015. We are conducting this trial at multiple clinical sites outside of the United States.

We enrolled two cohorts of patients with PNH in this trial at doses of 180 mg/day of APL-2 for the first cohort of two patients and 270 mg/day for the second cohort of three patients. In this clinical trial, doses of APL-2 were administered by subcutaneous injection for up to 28 consecutive days. Based on the evidence of safety and activity observed during the first 28 days of treatment, we extended the administration period for the patients in the second cohort to one year, and increased the number of patients who may be enrolled in the second cohort. As of February 28, 2018, APL-2 had been generally well tolerated in these patients, with six serious adverse events reported, each of which was considered unlikely to be related to administration of APL-2. In late October 2017, we learned that one patient with concomitant aplastic anemia developed bone marrow failure after one year of treatment with APL-2. Treatment with APL-2 was discontinued for this patient on November 14, 2017. The investigator determined that the bone marrow failure in this patient was not related to the administration of APL-2.

In the first cohort in this trial, two treatment-naïve patients with PNH completed 28 days of treatment with daily doses of 180 mg/day of APL-2 administered by subcutaneous injection. Reductions in LDH levels were observed in both patients from Day 1 to Day 29. Hemoglobin levels were maintained above 8.0 g/dL in both patients and neither required a transfusion during the treatment period. Both, however, required transfusions within four weeks of stopping APL-2.

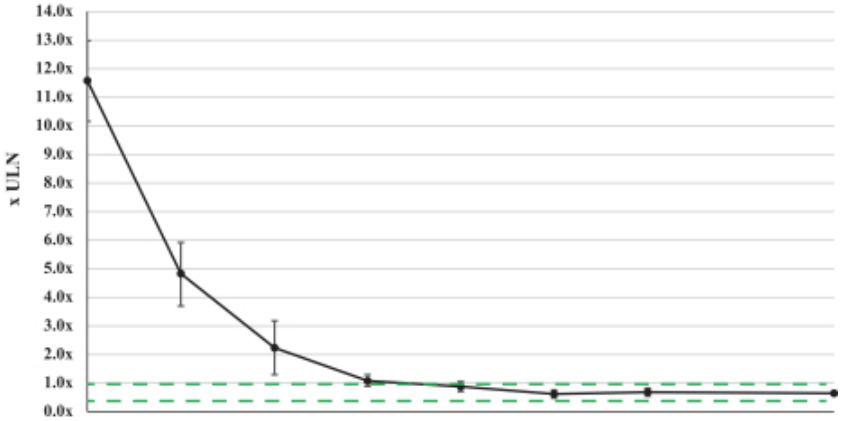
In the second cohort in this trial, three enrolled treatment-naïve patients completed the initial 28-day treatment period with daily doses of 270 mg/day of APL-2 administered by subcutaneous injection. All three patients demonstrated reductions in LDH levels to within two times the upper limit of normal. All patients treated

met the pre-determined criteria to continue dosing. Of the three patients, one discontinued dosing after developing bone marrow failure, one continued dosing for more than 300 days before withdrawing due to a diagnosis of metastatic ovarian cancer that was determined to be unrelated to APL-2, and one withdrew consent for personal reasons.

In the first quarter of 2018, we initiated enrollment of additional treatment-naive patients. In April 2018, we reported interim results as of April 13, 2018 of the Phase 1b trial in eight treatment-naive patients who had completed the initial 28-day treatment period with a daily dose of 270 mg of APL-2 as of April 13, 2018, the cut-off date for the interim data. These results exclude data from one of the original three patients, who had underlying metastatic ovarian cancer with a chronic low gastrointestinal bleed that was unknown at the time of screening for the trial, and which resulted in artificially low hemoglobin and high LDH levels that were determined to be unrelated to PNH, and also exclude data from the initial cohort of two patients that were treated with APL-2 at a dose of 180 mg/day.

The reported patients had a mean lactate dehydrogenase, or LDH, of 11.6 times the upper limit of normal at baseline which was reduced to a mean LDH of 0.9 times the upper limit of normal at day 28. The upper limit of normal range for LDH is 250 U/L. Seven of the eight patients were below the upper limit of normal at day 28. The graphic below shows the decrease in the mean LDH levels, as a multiple of the upper limit of normal, or ULN, over their respective treatment periods (up to the first eight weeks) in the eight reported patients who received a daily dose of 270 mg of APL-2 and were treated for at least 28 days.

Mean LDH

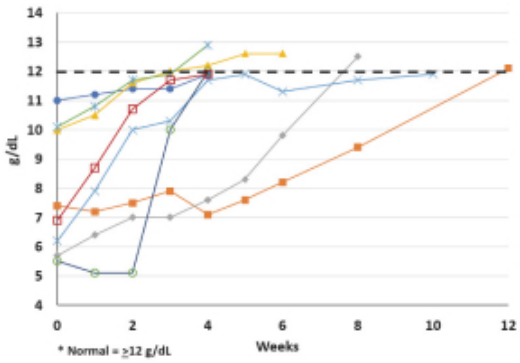


Week	0	1	2	3	4	5	6	7	8
Number	n=8	n=8	n=8	n=8	n=8	n=4	n=4	Not Taken	n=3
Multiple of ULN	11.58x	4.82x	2.25x	1.09x	0.90x	0.62x	0.69x		0.65x

As of April 13, 2018, the eight reported patients had an average increase in hemoglobin of 4.3 g/dL from a baseline average of 7.9 g/dL to an average last measurement of 12.2 g/dL within the first 12 weeks of the treatment period. The lower limit of the normal range for hemoglobin is 12 g/dL. Except for two patients, each of whom received a single transfusion within the first two weeks of treatment with APL-2, no other transfusions have been reported in the trial for any patients during the treatment period. The graphic below shows the measurement of hemoglobin levels for each of the reported patients over their respective treatment periods (up to 12 weeks).

Table of Contents

Hemoglobin

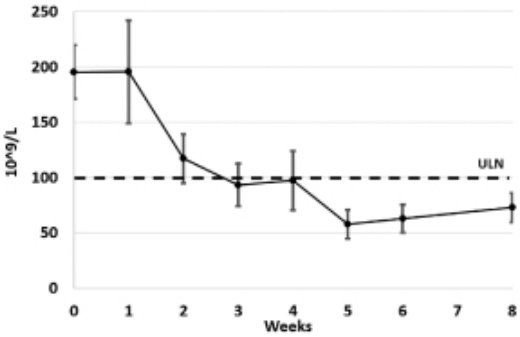


	Individual Hgb Levels		
	Baseline	Most Recent	Week
Patient 1	11.0	11.9	Week 4
Patient 2	7.4	12.1	Week 12(1)
Patient 3	5.7	12.5	Week 8
Patient 4	10.0	12.6	Week 6
Patient 5	6.2	11.9	Week 10
Patient 6	10.1	12.9	Week 4
Patient 7	5.5	12.0	Week 4
Patient 8	6.9	11.9	Week 4
Average	**7.9**	**12.2**	

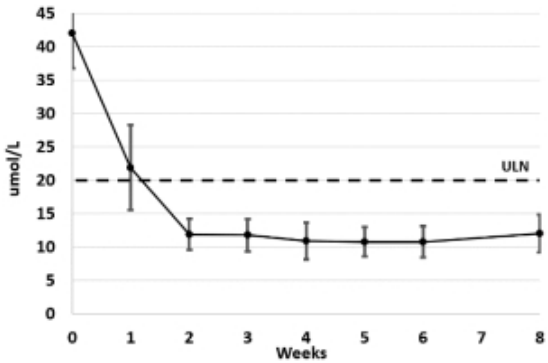
(1) Patient 2 has been dosed beyond week 12

These eight patients had an average reduction in absolute reticulocyte count of 50% from 195 10^9/L to 97 10^9/L at day 28. Normal reticulocyte count is 30 to 100 10^9/L. The patients also had an average reduction in bilirubin of 74% from an average baseline of 42 umol/L to an average of 11 umol/L at day 28. Normal bilirubin level is 3 to 20 umol/l. The graphic below shows the decreases in average reticulocyte count and average bilirubin level in the first eight weeks of treatment.

Mean Reticulocytes



Mean Total Bilirubin



Weeks	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Number of Patients	**n=8**	**n=8**	**n=8**	**n=8**	**n=8**	**n=4**	**n=4**	**Not Taken**	**n=3**
Mean Reticulocytes (10^9/L)	**195**	**195**	**117**	**93**	**97**	**58**	**63**		**73**

Mean Bilirubin (umol/L)	**42**	**22**	**12**	**12**	**11**	**11**	**11**	**12**

APL-2 has generally been well tolerated in the reported patients. We have not observed any significant infections or thromboembolic events. We plan to continue enrolling treatment-naive patients in this trial and plan to report additional data in June 2018.

Supporting Trials

We are conducting a Phase 1 trial to assess the safety and tolerability of APL-2 in patients with renal impairment. The study will initially include one cohort of eight patients with severe renal impairment and a second cohort of eight control patients and will evaluate various PK endpoints, in addition to safety and tolerability endpoints.

We are conducting a Phase 1 trial to determine the safety, PK and PD of twice-weekly and once-weekly subcutaneous administration of APL-2 in healthy volunteers. We intend to evaluate whether less frequent administration provides comparable PK and PD profiles to daily subcutaneous administration and may enable less frequent dosing in upcoming clinical trials.

We are conducting a Phase 1 trial to determine the safety, PK and PD of APL-2 in healthy volunteers of Japanese descent. We intend to evaluate whether APL-2 will have comparable PK and PD profiles in this population.

We plan to initiate long-term safety extension trials in the second half of 2018 to support subcutaneous dosing with APL-2 for patients with PNH who have previously participated in a clinical trial with APL-2.

We discontinued the single-center, observational, prospective natural history study of patients with PNH.

Completed Phase 1 Clinical Trials—Single and Multiple Ascending Dose in Healthy Volunteers

We have completed both single ascending and multiple ascending dose Phase 1 randomized, double-blind, placebo-controlled clinical trials of APL-2 in healthy volunteers. We conducted the trials at a single site in Australia to assess the safety, tolerability, PK and PD of APL-2.

In the Phase 1 single ascending dose trial, APL-2 was administered by subcutaneous injection to healthy volunteers on the first day of the trial and followed by either 29 or 43 days of monitoring depending on dosing level. We enrolled 31 subjects in this trial. These subjects participated in one of six cohorts at doses ranging from 45 mg to 1440 mg. In the Phase 1 multiple ascending dose trial, APL-2 was administered by subcutaneous injection to healthy volunteers daily for 28 consecutive days followed by 56 days of monitoring after last dosing. We enrolled 20 subjects in this trial. These subjects participated in one of four cohorts at doses ranging from 30 mg to 270 mg/day.

A total of 24 subjects received single doses of APL-2 at doses up to 1440 mg and 16 subjects received multiple doses of APL-2 for 28 consecutive days at doses up to 270 mg/day. A total of 11 subjects received either single or multiple administrations of a placebo in these trials.

We observed the following in the trials:

- APL-2 was well tolerated in both trials with no serious adverse events reported;
- the PK of APL-2 in humans was in line with our expectations derived from preclinical data, with little inter-subject variability observed;
- in the multiple ascending dose trial, the plasma concentration of APL-2 increased over time, reaching maximum concentration after the last day of administration on day 28; and
- in both trials, we observed a dose-dependent increase in C3 that is indicative of APL-2 binding to C3.

In these trials, we assessed inhibition of hemolysis of red blood cells by using *ex vivo* serum-induced hemolysis. In the multiple ascending dose trial, at a dose level of 180 mg/day of APL-2, reduction of *ex vivo* serum-induced hemolysis was observed as early as seven days after initiation of treatment, continued for the duration of treatment, and reached a maximum of more than 80% in two of the four subjects who received 180/mg day of APL-2 and of more than 60% in the other two subjects. At the dose level of 270 mg/day of APL-2, reduction of *ex vivo* serum-induced hemolysis was observed as early as seven days after initiation of treatment, continued for the duration of treatment, and reached a maximum reduction of more than 90% in three of the four subjects who received 270 mg/day of APL-2. The fourth subject on active treatment had a more moderate reduction compared to placebo.

Preclinical Studies

We have conducted numerous preclinical studies of APL-2 in animals and in laboratory samples to assess the safety of APL-2, including repeat-dose subcutaneous and intravenous toxicity studies of APL-2 in rats, rabbits and monkeys for durations of up to nine months. In these studies, there were no significant macroscopically observable or clinical pathology drug-related changes in any species at any of the doses tested. Similarly, there was no evidence of a potential for adverse effects on myocardial conduction, cardiovascular and respiratory systems in either species and no genotoxicity potential was observed. In addition, no signs of infection were observed in any of the studies that we conducted. The main toxicity observed at the highest doses tested was microscopic kidney damage, likely resulting from accumulation of APL-2 in the kidney, which is one of the organs we believe to be responsible for its clearance from the body.

While there is no animal model of PNH, APL-2 inhibited both hemolysis of red blood cells by the membrane attack complex and C3 fragment deposition on the surface of these cells in preclinical studies that we conducted *ex vivo* on blood samples from patients with PNH.

Autoimmune Hemolytic Anemia (Systemic APL-2)

Autoimmune hemolytic anemia, or AIHA, comprises a group of rare, autoimmune diseases characterized by autoantibody-initiated premature destruction of red blood cells and classified by the type of immunoglobulin involved in causing the disease and its thermal optimum for binding red blood cells. Complement plays a major role in red blood cell destruction in AIHA through extravascular hemolysis, which corresponds to the removal and destruction of opsonized red blood cells from the blood vessels by the spleen or liver, and intravascular hemolysis, which corresponds to the destruction of the red blood cells following the formation of the membrane attack complex in the membrane of the red blood cells in the blood vessels. We are developing APL-2 as a therapy for two subtypes of AIHA: cold agglutinin disease, or CAD, and warm antibody AIHA, or wAIHA.

There is no FDA-approved drug therapy specifically for either subtype of AIHA. The primary and secondary therapies, which include corticosteroids, splenectomy, alkylating agents and immunosuppressive drugs, are associated with low response rates, relapses and clinically significant adverse effects.

We believe that C3 inhibition has the potential to prevent C3-related opsonization and extravascular hemolysis in AIHA patients, and that inhibiting the complement system by targeting C3 may have the same impact, if not greater, as other complement pathway drugs in these diseases.

We plan to initiate a Phase 2 open-label, prospective, 12-month trial in patients with a primary diagnosis of wAIHA or CAD in the first half of 2018 to assess safety, tolerability and preliminary evidence of activity of C3 complement inhibition with APL-2 in these patients. We plan to enroll 12 patients, six patients with wAIHA in cohort 1 and six patients with CAD in cohort 2. Patients in each cohort will receive either 270 mg/day or 360 mg/day of APL-2 treatment for up to 12 months. Dose escalation from 270 mg/day to 360 mg/day or de-escalation from 360 mg/day to 270 mg/day may occur after thorough evaluation of available safety and laboratory assessment. Primary efficacy endpoints will include change from baseline hemoglobin levels, number of red blood cell transfusions during the trial, change from baseline in absolute reticulocyte count, LDH, haptoglobin, indirect bilirubin, APL-2 serum concentration and other PK parameters, change in quality of life scores, and measurements of complement levels and C3 deposition on red blood cells. This trial will be conducted under our existing IND for PNH. We plan to report data from these patients in the second quarter of 2018.

Nephrology (systemic APL-2)

Complement-Dependent Nephropathies

IgA nephropathy, or IgAN, lupus nephritis, idiopathic membranous nephropathy and C3 glomerulopathy are diseases caused by activation of complement pathways. In all of these diseases, immune complexes

(autoantibody-antigen complexes) or C3 are deposited in the portion of the kidney known as the glomeruli, which is responsible for blood filtration. These deposits lead to activation of either all three or two of the three principal pathways of the complement system: classical, lectin and alternative. By targeting C3 at the point of convergence of all three pathways, we believe APL-2 has the potential to prevent C3 activation and C3-mediated inflammatory response responsible for the renal manifestations of injury common to all these diseases. We met with the FDA in October 2017 in a pre-IND meeting and submitted an IND to the FDA in November 2017.

We plan to initiate a single prospective open label Phase 2 clinical trial in patients who have been clinically diagnosed with IgA nephropathy (IgAN), lupus nephritis, idiopathic membranous nephropathy or C3 glomerulopathy in the first half of 2018 to evaluate safety and preliminary activity of APL-2 in patients with these complement-dependent nephropathies. We plan to enroll up to 12 patients per disease. The clinical diagnosis for each patient must be confirmed by renal biopsy prior to dosing with APL-2. Each patient will receive once daily subcutaneous infusions of up to 360 mg of APL-2 for 16 weeks. The primary efficacy endpoint will be the reduction in proteinuria from baseline to week 16. Based on the scientific literature, a substantial reduction in proteinuria would be reasonably likely to predict a clinical benefit in IgAN. Proteinuria was accepted by the FDA as surrogate for all diseases in this trial. We plan to report data from these patients in the second half of 2018.

Other Complement-Dependent Diseases

We are developing APL-9 for intravenous administration in systemic indications. We are conducting a single ascending dose Phase 1 randomized, double-blind, placebo-controlled clinical trials of APL-9 in healthy volunteers. This trial will enable us to determine the safety, PK and PD of APL-9. In this trial, APL-9 will be administered by an intravenous infusion of approximately 30 minutes to healthy volunteers on the first day of the trial and followed by eight days of monitoring. We plan to enroll 24 subjects in this trial. Subjects will participate in one of four cohorts. The starting dose for the first cohort will be 30 mg of APL-9 and we will determine the doses for the subsequent cohorts after safety review by a safety monitoring committee.

Systemic Administration Drug Delivery System

In our clinical trials, we are currently using an off-the-shelf, FDA-cleared device that enables patients to self-administer APL-2 through subcutaneous infusion. In addition, we are developing, with a third-party manufacturer, a custom, on-body drug delivery system that would further improve the ease of self-administration of APL-2. While our goal is to commercially launch APL-2 in PNH together with the custom drug delivery system, we can commercialize APL-2 without the custom drug delivery system, in which case marketing approval for APL-2 will not be contingent upon approval of the drug delivery system.

Intellectual Property

Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. We seek to protect our proprietary position in a variety of ways, including by pursuing patent protection in certain jurisdictions where it is available. For example, we file U.S. and certain foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

We have developed our lead product candidate, APL-2, which is an analog of the cyclic peptide compstatin, based on technology that we have exclusively licensed from the Trustees of the University of Pennsylvania, or Penn, including a license agreement with Penn that was assigned to us in connection with our acquisition of the assets of Potentia in September 2015. The intellectual property in-licensed under our two license agreements with Penn includes four U.S. patents and two pending U.S. patent applications, including original filings,

continuations and divisional applications, and numerous foreign counterparts, with claims granted or pending in Europe, Japan and elsewhere. These licensed patent rights include issued patents with claims that recite a class of compounds generically covering our lead product candidate, APL-2, and that specifically recite the active component. These patents have terms that extend to 2026.

In addition to the intellectual property licensed from Penn, as of December 31, 2017, we own a total of six U.S. patents and 19 pending U.S. patent applications, including original filings, continuations and divisional applications, as well as numerous foreign counterparts of many of these patents and patent applications. Our patent applications include families of US and foreign applications relating, for example, to certain compstatin analogs with a prolonged *in vivo* half-life, including APL-2, and/or to methods of treatment and dosing regimens for treating particular complement-dependent diseases. Patents issuing from these applications would expire in 2032 or 2033. Our patent applications also include families relating in part to particular doses and dosing regimens for intravitreally or subcutaneously administered APL-2. Patents based on these applications would expire between 2036 and 2038. Finally, the filings include certain U.S. and foreign patents and patent applications relating to methods of treating eye disorders associated with complement activation, which we acquired in the acquisition of Potentia's assets. These acquired Potentia patent rights include issued U.S. patents with claims to methods of treating AMD by administration of compstatin analogs and a granted European patent with claims to a class of compstatin analogs for use in treatment of macular degeneration. These patents have terms that extend into 2026.

The term of individual patents depends upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, the patent term is generally 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country. In the United States, a patent's term may, in certain cases, be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over a commonly owned patent or a patent naming a common inventor and having an earlier expiration date. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration date of a U.S. patent as partial compensation for the length of time the drug is under regulatory review while the patent is in force. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended.

Similar provisions are available in the European Union and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our product candidates, including APL-2, receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those products, depending upon the length of the clinical trials for each drug and other factors. Expiration dates referred to above are without regard to potential patent term adjustment or extension or other market exclusivity that may be available to us.

We granted rights to use our intellectual property to manage our Phase 1 and 2 clinical trials in Australia and exclusive rights to distribute our product within Australia, South Korea, Singapore, Indonesia, Malaysia, the Philippines, Thailand, Vietnam and New Zealand to our wholly-owned subsidiary, Apellis Australia Pty Ltd.

We may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

Patent License Agreement with The Trustees of the University of Pennsylvania (Non-ophthalmic Fields of Use)

In March 2008, Apellis AG entered into an agreement with Penn for an exclusive worldwide license, under specified patent rights controlled by Penn, to develop and commercialize products covered by the licensed patent rights for all fields except the treatment of ophthalmic indications. This license was assigned to us in 2010 in connection with our acquisition of Apellis AG, and we have the right to grant sublicenses under this license.

The patent rights licensed to us by Penn include patents with claims that recite a class of compounds generically covering our lead compound, APL-2, and specifically recite APL-1.

In exchange for the rights licensed from Penn, Apellis AG transferred to Penn shares of Potentia common stock that it had purchased from Potentia with a $250,000 promissory note in 2008. In 2010, Apellis AG assigned its Penn license to us together with the promissory note. We repaid the promissory note in full in 2013.

Under the license agreement, we are obligated to make a $100,000 annual license maintenance payment to Penn until the first commercial sale of a licensed product, some of which may become creditable against milestone payments under specified circumstances. We may also become obligated to make payments to Penn aggregating up to $1,650,000 based on achieving specified development and regulatory approval milestones and up to $2,500,000 based on achieving specified annual sales milestones with respect to each of the first two licensed products, and to pay low single-digit royalties to Penn based on net sales of each licensed product by us and our affiliates and sublicensees and specified minimum quarterly royalty thresholds. In addition, we are obligated to pay Penn a specified portion of income we receive from sublicensees.

Our royalty obligation with respect to each licensed product in a country extends until the later of the expiration of the last-to-expire patent licensed from Penn covering the licensed product in the country or the expiration of a specified number of years after the first commercial sale of the licensed product in the country.

The agreement obligates us to use commercially reasonable efforts to develop licensed products in accordance with a development plan, which we update annually, and a development milestone timetable specified in the agreement and to use commercially reasonable efforts to commercialize licensed products.

Penn has the right to terminate the agreement if we breach the agreement and fail to cure our breach within specified cure periods or in the event of specified bankruptcy, insolvency and liquidation events. We have the right to terminate the agreement for our convenience at any time on 60 days' notice to Penn.

Amended and Restated Patent License Agreement with The Trustees of the University of Pennsylvania (Ophthalmic Field of Use)

At the same time that it entered into the agreement with Apellis AG, Penn licensed rights to the same portfolio of cases to Potentia, to develop and commercialize products covered by the licensed patent rights for the treatment of ophthalmic indications. In September 2015, Potentia assigned the license agreement between Potentia and Penn to us in connection with our acquisition of the assets of Potentia pursuant to an asset purchase agreement with Potentia.

Upon Potentia's assignment of the license to us, we became the licensee and are obligated to make a $100,000 annual license maintenance payment to Penn until the first commercial sale of a licensed product. We also became obligated to make payments to Penn aggregating up to $3,200,000 based on achieving specified development and regulatory approval milestones and up to $5,000,000 based on achieving specified annual sales milestones with respect to each licensed product, and to pay low single-digit royalties to Penn based on net sales of each licensed product by us and our affiliates and sublicensees and specified minimum quarterly royalty thresholds. In addition, we are obligated to pay Penn a specified portion of income we receive from sublicensees.

Our royalty obligation with respect to each licensed product in a country will extend until the later of the expiration of the last-to-expire patent licensed from Penn covering the licensed product in the country or the tenth anniversary of the first commercial sale of the licensed product in the country.

We have the right to grant sublicenses under the license.

We also are obligated to use commercially reasonable efforts to develop licensed products in accordance with a development plan, which we will update annually, and a development milestone timetable specified in the agreement and to use commercially reasonable efforts to commercialize licensed products.

Penn has the right to terminate the agreement if we breach the agreement and fail to cure our breach within specified cure periods or in the event of specified bankruptcy, insolvency and liquidation events. We have the right to terminate the agreement for our convenience at any time on 60 days' notice to Penn.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technologies, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

There are a number of currently marketed products and product candidates in preclinical research and clinical development by third parties to treat the various diseases that we are targeting. In general, these products and product candidates can be categorized based on their proposed mechanisms of action. The mechanisms of action for these product candidates include inflammation suppression by agents such as complement inhibitors and corticosteroids, as well as immune modulators, visual cycle modulators, anti-amyloid agents, antioxidants, neuroprotectants, cell and gene therapies and vascular and interstitial tissue remodeling agents.

If our lead product candidate is approved for the indications for which we are currently undertaking or planning clinical trials, it will compete with the products and product candidates discussed below.

GA. There are currently no approved treatments for GA. We are aware that there are a number of companies that are actively developing product candidates for the treatment of GA, including the following product candidates that are in clinical development: CLG561, an anti-properdin monoclonal antibody being developed as a monotherapy or adjunctive therapy with LFG316, an anti-C5 monoclonal antibody being developed by Novartis AG that is in Phase 2 clinical trials; Zimura, a C5 inhibitor being developed by Ophthotech Corporation that is in Phase 2/3 clinical trials; and other product candidates that do not target the complement system that are in Phase 2 clinical trials, including compounds being developed by Allergan PLC and Regenerative Patch Technologies. In September and November 2017, Roche announced that its Phase 3 trials of lampalizumab in GA had failed to meet its primary endpoint.

PNH. Eculizumab, a C5 complement inhibitor, which is marketed as Soliris by Alexion Pharmaceuticals, Inc., is the only drug approved for the treatment of PNH. Alexion is also developing ALXN1210 for patients with PNH which is currently in Phase 3 trials. ALXN1210 is designed to have a longer half-life and greater inhibition of C5 than eculizumab. In addition, we are aware that there are a number of other companies that are actively developing product candidates for the treatment of PNH, including the following:

- a product candidate directed at C3 complement inhibition that is currently in Phase 1 clinical development by Amyndas Pharmaceuticals SA;

- product candidates directed at C5 complement inhibition such as ALN-CC5, an RNAi therapeutic targeting C5 being developed by Alnylam Pharmaceuticals, Inc. that is in early clinical trials, Coversin, a small protein inhibitor of C5 being developed by Akari Therapeutics, Plc. that is in Phase 2 clinical trials, Ra101495, a cyclic peptide inhibitor of C5 that is currently in Phase 2 development by Ra Pharmaceuticals, Inc., and LFG316, an anti-C5 monoclonal antibody that is currently in Phase 2 trials by Novartis;
- other product candidates directed at other mechanisms of complement inhibition such as NM-9405, an anti-properdin antibody in preclinical development by NovelMed Therapeutics, Inc., and ACH-4471 (previously ACH-CFDIS), an orally available small molecule inhibitor of complement factor D, that is currently in early clinical development by Achillion Pharmaceuticals, Inc.; and
- Amgen is developing ABP959, a biosimilar for eculizumab that is in early clinical development.

AIHA. There are no currently marketed drug treatments for AIHA, but there are currently treatments in development for AIHA, including:

- Fostamatinib, a spleen tyrosine kinase inhibitor being developed by Rigel Pharmaceuticals, Inc. is now in Phase 2 trials in AIHA patients; and
- TNT-009/BIVV009, a C1s monoclonal antibody inhibitor, which is being developed by Bioverativ Inc., and is in early clinical trials in patients with CAD.

Complement-Dependent Nephropathies. There are no currently marketed drug treatments for complement-dependent nephropathies, but OMS721, a human monoclonal antibody to mannose-binding lectin-associated serine protease-2 (MASP-2) that blocks the lectin pathway, is being developed by Omeros Corp. as a treatment for IgAN and is entering Phase 3 clinical trials.

Sales and Marketing

We hold worldwide commercialization rights to all our product candidates. We plan to build focused capabilities to commercialize development programs for certain indications where we believe that the medical specialists for the indications are sufficiently concentrated to allow us to effectively promote the product with a targeted sales team. In other indications, we may seek to enter into collaborations that we believe may contribute to our ability to advance development and ultimately commercialize our product candidates. We may also seek to enter into collaborations where we believe that realizing the full commercial value of our development programs will require access to broader geographic markets or the pursuit of broader patient populations or indications.

Manufacturing

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates. Although we intend to rely on third-party contract manufacturers to produce our products, we have recruited personnel with experience to manage the third-party contract manufacturers producing our product candidates and other product candidates or products that we may develop in the future.

The process for manufacturing our product candidates consists of chemical synthesis, purification using liquid chromatography, and freeze drying into solid form. Each of these steps involves a relatively routine chemical engineering process. We expect the costs associated with manufacturing drug substance for our product candidates may be comparable to the current manufacturing costs for other similarly sized peptide-based components.

We have engaged a limited number of third-party manufacturers to provide all of our raw materials, drug substances and finished products for use in clinical trials. Our raw materials, drug substances and finished products have been produced under master service contracts and specific work orders from these manufacturers

pursuant to agreements that include specific supply timelines and volume and quality expectations. We choose the third-party manufacturers of the raw materials and drug substances based on the volume required and the regulatory requirements at the relevant stage of development. All lots of drug substances and finished products used in clinical trials are manufactured under current good manufacturing practices. A separate third-party manufacturer has been responsible for fill and finish services and for labeling and shipment of the final drug products to the clinical trial sites.

Government Regulation and Product Approvals

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

Review and Approval of Drugs in the United States

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The failure to comply with applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities, including state agencies.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of a new drug application, or NDA;
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the NDA; and

- compliance with any post-approval requirements, including Risk Evaluation and Mitigation Strategies, or REMS, and post-approval studies required by the FDA.

Preclinical Studies

Before an applicant begins testing a product candidate with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or active pharmaceutical ingredient and the formulated drug or drug product, as well as *in vitro* and animal studies to assess the safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

Companies usually must complete some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and must also develop additional information about the chemistry and physical characteristics of the investigational product and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved NDA. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When the

foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain FDA requirements in order to use the study as support for an IND or application for marketing approval. Those requirements provide that such studies must be conducted in accordance with GCP, including review and approval by an independent ethics committee, or IEC, and informed consent from subjects.

In addition to the IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website.

Human Clinical Studies in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in the following sequential phases, which may overlap or be combined:

- Phase 1: The drug is initially introduced into healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.
- Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.
- Phase 4: Post-approval studies, which are conducted following initial approval, are typically conducted to gain additional experience and data from treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for

any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality, purity, and potency of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2018 is $2,421,495 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for federal fiscal year 2018 is $304,162. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and strives to inform the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to certain performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the date of filing, and most applications for "priority review" products are meant to be reviewed within six months of filing. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including drug component manufacturing (such as active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities comply with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Under the FDA Reauthorization Act of 2017, or FDARA, the FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain drug applications, including applications for drugs in a shortage or drugs for which approval is dependent on remediation of conditions identified in the inspection report.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

The FDA may refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy, Priority Review and Regenerative Advanced Therapy Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, priority review and regenerative advanced therapy designation.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the application is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction,

documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Fourth, with passage of the 21st Century Cures Act, or the Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. There is limited experience with accelerated approvals by the FDA based on intermediate clinical endpoints. However, the FDA has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter.

An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, healthcare professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, the FDA's regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementation regulations, as well as the Drug Supply Chain Security Act, or DSCSA, which regulates the distribution of and tracing of prescription drugs and prescription drug samples at the federal level, and sets minimum standards for the regulation of drug distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCSA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug..."

Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data

exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

Under FDARA, a priority review track will be established for certain generic drugs, requiring the FDA to review a drug application within eight months for a drug that has three or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The new legislation also authorizes the FDA to expedite review of "competitor generic therapies" or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the ANDA applicant is not seeking approval).

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for

filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the Food and Drug Safety and Innovation Act, or the FDASIA, in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time. For drugs intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of an applicant, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments.

In addition, FDARA requires the FDA to meet early in the development process to discuss pediatric study plans with drug sponsors. The legislation requires the FDA to meet with drug sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than 90 days after the FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application. With regard to patents, the six-month pediatric exclusivity period will not attach to any patents for which a generic (ANDA or 505(b)(2) NDA) applicant submitted a paragraph IV patent certification, unless the NDA sponsor or patent owner first obtains a court determination that the patent is valid and infringed by a proposed generic product.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the

product). A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will be receiving orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. Those circumstances include instances in which another sponsor's application for the same drug product and indication is shown to be "clinically superior" to the previously approved drug. In this context, clinically superior means that the drug provides a significant therapeutic advantage over and above the already approved drug in terms of greater efficacy, greater safety or by providing a major contribution to patient care. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity.

Under FDARA, orphan exclusivity will not bar approval of another orphan drug under certain circumstances, including if a subsequent product with the same drug for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan exclusivity regardless of a showing of clinical superiority.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Review and Clearance or Approval of Medical Devices in the United States

Medical devices in the United States are strictly regulated by the FDA. Under the FDCA, a medical device is defined as an instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent, or other similar or related article, including a component part, or accessory which is, among other things: intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes. This definition provides a clear distinction between a medical device and other FDA regulated products such as drugs. If the primary intended use of the product is achieved through chemical action or by being metabolized by the body, the product is usually a drug. If not, it is generally a medical device.

Unless an exemption applies, a new medical device may not be marketed in the United States until it has been cleared through filing of a 510(k) premarket notification, or 510(k), or approved by the FDA pursuant to a

premarket approval application, or PMA. The information that must be submitted to the FDA in order to obtain clearance or approval to market a new medical device varies depending on how the medical device is classified by the FDA. Medical devices are classified into one of three classes on the basis of the controls deemed by the FDA to be necessary to reasonably ensure their safety and effectiveness. Class I devices have the lowest level or risk associated with them, and are subject to general controls, including labeling, premarket notification and adherence to the Quality System Regulation, or QSR. Class II devices are subject to general controls and special controls, including performance standards. Class III devices, which have the highest level of risk associated with them, such as life sustaining, life supporting or some implantable devices, or devices that have a new intended use, or use advanced technology that is not substantially equivalent to that of a legally marketed device, are subject to most of the aforementioned requirements as well as to premarket approval.

A 510(k) must demonstrate that the proposed device is substantially equivalent to another legally marketed device, or predicate device, that did not require premarket approval. In evaluating a 510(k), the FDA will determine whether the device has the same intended use as the predicate device, and (a) has the same technological characteristics as the predicate device, or (b) has different technological characteristics, and (i) the data supporting substantial equivalence contains information, including appropriate clinical or scientific data, if deemed necessary by the FDA, that demonstrates that the device is as safe and as effective as a legally marketed device, and (ii) does not raise different questions of safety and effectiveness than the predicate device. Most 510(k)s do not require clinical data for clearance, but the FDA may request such data. The FDA seeks to review and act on a 510(k) within 90 days of submission, but it may take longer if the agency finds that it requires more information to review the 510(k). If the FDA concludes that a new device is not substantially equivalent to a predicate device, the new device will be classified in Class III and the manufacturer will be required to submit a PMA to market the product.

Modifications to a 510(k)-cleared medical device may require the submission of another 510(k) or a PMA if the changes could significantly affect safety or effectiveness or constitute a major change in the intended use of the device. Modifications to a 510(k)-cleared device frequently require the submission of a traditional 510(k), but modifications meeting certain conditions may be candidates for FDA review under a Special 510(k). If a device modification requires the submission of a 510(k), but the modification does not affect the intended use of the device or alter the fundamental technology of the device, then summary information that results from the design control process associated with the cleared device can serve as the basis for clearing the application. A Special 510(k) allows a manufacturer to declare conformance to design controls without providing new data. When the modification involves a change in material, the nature of the “new” material will determine whether a traditional or Special 510(k) is necessary.

Review and Approval of Combination Products in the United States

Certain products may be comprised of components that would normally be regulated under different types of regulatory authorities, and frequently by different Centers at the FDA. These products are known as combination products. Under regulations issued by the FDA, a combination product may be:

- a product comprised of two or more regulated components that are physically, chemically, or otherwise combined or mixed and produced as a single entity;
- two or more separate products packaged together in a single package or as a unit and comprised of drug and device products;
- a drug or device packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug or device where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or

- any investigational drug or device packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

Under the FDCA, the FDA is charged with assigning a center with primary jurisdiction, or a lead center, for review of a combination product. That determination is based on the "primary mode of action" of the combination product. Thus, if the primary mode of action of a device-drug combination product is attributable to the drug product, the FDA Center responsible for premarket review of the drug product would have primary jurisdiction for the combination product. The FDA has also established an Office of Combination Products to address issues surrounding combination products and provide more certainty to the regulatory review process. That office serves as a focal point for combination product issues for agency reviewers and industry. It is also responsible for developing guidance and regulations to clarify the regulation of combination products, and for assignment of the FDA center that has primary jurisdiction for review of combination products where the jurisdiction is unclear or in dispute.

Review and Approval of Drug Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Procedures Governing Approval of Drug Products in the European Union

Pursuant to the European Clinical Trials Directive, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of an E.U. member state in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial after a competent ethics committee has issued a favorable opinion. Clinical trial application must be accompanied by an investigational medicinal product dossier with supporting information prescribed by the European Clinical Trials Directive and corresponding national laws of the member states and further detailed in applicable guidance documents.

To obtain marketing approval of a product under European Union regulatory systems, an applicant must submit a marketing authorization application, or MAA, either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all E.U. member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the European Medicines Agency, or EMA, is responsible for conducting the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the

assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure is available to applicants who wish to market a product in various E.U. member states where such product has not previously received marketing approval in any E.U. member states. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state designated by the applicant, known as the reference member state. Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 210 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the European Commission, whose decision is binding on all member states.

Clinical Trial Approval

Requirements for the conduct of clinical trials in the European Union including Good Clinical Practice, or GCP, are set forth in the Clinical Trials Directive 2001/20/EC and the GCP Directive 2005/28/EC. Pursuant to Directive 2001/20/EC and Directive 2005/28/EC, as amended, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the E.U. member states. Under this system, approval must be obtained from the competent national authority of each E.U. member state in which a study is planned to be conducted. To this end, a clinical trial application is submitted, which must be supported by an investigational medicinal product dossier, or IMPD, and further supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and other applicable guidance documents. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the clinical trial application in that country.

In April 2014, the European Union passed the new Clinical Trials Regulation, (EU) No 536/2014, which will replace the current Clinical Trials Directive 2001/20/EC. The Regulation was published on June 16, 2014 but is not expected to apply until 2019. To ensure that the rules for clinical trials are identical throughout the European Union, the new E.U. clinical trials legislation was passed as a regulation that is directly applicable in all E.U. member states. All clinical trials performed in the European Union are required to be conducted in accordance with the Clinical Trials Directive 2001/20/EC until the new Clinical Trials Regulation (EU) No 536/2014 becomes applicable. The Clinical Trials Directive 2001/20/EC will, however, still apply three years from the date of entry into application of the Clinical Trials Regulation to (i) clinical trials applications submitted before the entry into application and (ii) clinical trials applications submitted within one year after the entry into application if the sponsor opts for old system.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trial in the European Union. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the E.U. portal; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures that will spare sponsors from submitting broadly identical information separately to various bodies and different member states; a harmonized procedure for the assessment of

applications for clinical trials, which is divided in two parts—Part I is assessed jointly by all member states concerned. Part II is assessed separately by each member state concerned; strictly defined deadlines for the assessment of clinical trial applications; and the involvement of the ethics committees in the assessment procedure in accordance with the national law of the member state concerned but within the overall timelines defined by the Clinical Trials Regulation.

PRIME Designation in the EU

In March 2016, the EMA launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises, or SMEs, may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated Agency contact and rapporteur from the CHMP or Committee for Advanced Therapies are appointed early in PRIME scheme facilitating increased understanding of the product at EMA's Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Data and Market Exclusivity in the European Union

In the European Union, new chemical entities qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application for eight years, after which generic marketing authorization can be submitted, and the innovator's data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity and the sponsor is able to gain the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company can complete a full MAA with a complete database of pharmaceutical tests, preclinical tests and clinical trials and obtain marketing approval of its product.

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Periods of Authorization and Renewals

Marketing authorization is valid for five years in principle and the marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent

authority of the authorizing member state. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. Any authorization which is not followed by the actual placing of the drug on the European Union market (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid (the so-called sunset clause).

Orphan Drug Designation and Exclusivity

Regulation 141/2000 provides that a drug shall be designated as an orphan drug if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Community when the application is made, or that the product is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the European Community and that without incentives it is unlikely that the marketing of the drug in the European Community would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Community or, if such method exists, the drug will be of significant benefit to those affected by that condition.

Regulation 847/2000 sets out criteria and procedures governing designation of orphan drugs in the European Union. Specifically, an application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. This period may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation, for example because the product is sufficiently profitable not to justify market exclusivity. Market exclusivity can be revoked only in very selected cases, such as consent from the marketing authorization holder, inability to supply sufficient quantities of the product, demonstration of “clinically relevant superiority” by a similar medicinal product, or, after a review by the Committee for Orphan Medicinal Products, requested by a member state in the fifth year of the marketing exclusivity period (if the designation criteria are believed to no longer apply). Medicinal products designated as orphan drugs pursuant to Regulation 141/2000 shall be eligible for incentives made available by the European Community and by the member states to support research into, and the development and availability of, orphan drugs.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom (U.K.) voted in favor of leaving the European Union (commonly referred to as “Brexit”). Thereafter, on March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The withdrawal of the U.K. from the European Union will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the U.K. provides a notice of withdrawal pursuant to the E.U. Treaty. Since the regulatory framework for pharmaceutical products in the U.K. covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the U.K. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the U.K.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such products. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. Additionally, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for our product candidates will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of our product candidates or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has

price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted regulatory approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain our business and/or financial arrangements. Such restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease or order of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willingly executing, or attempting to execute, a scheme or making false statements in connection with the delivery of or payment for health care benefits, items, or services;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, which also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information on covered entities and their business associates that associates that perform certain functions or activities that involve the use or disclosure of protected health information on their behalf;
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or collectively the ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the U.S. Department of Health and Human Services, information related to payments and other transfers of value to physicians and teaching hospitals and information regarding ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Healthcare Reform

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

In March 2010, the United States Congress enacted the Affordable Care Act, or ACA, which, among other things, includes changes to the coverage and payment for drug products under government health care programs. Among the provisions of the ACA of importance to our potential product candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% (and 70% starting January 1, 2019) point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments, will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal

year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called “Cadillac” tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, among other things, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole”. The Congress will likely consider other legislation to replace elements of the ACA, during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the ACA exchanges. At the same time, the Administration announced that it will discontinue the payment of cost-sharing reduction, or CSR, payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA.

A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain. We will continue to evaluate the effect that the ACA and its possible repeal and replacement could have on our business.

Further, there have been several recent U.S. congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration’s budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

Scientific Advisory Boards

Our scientific advisory board includes physicians and scientists recognized as authorities in the areas of hematology, neurology, ophthalmology and pulmonology. Our scientific advisory board meets annually and provides scientific and clinical insights and strategic guidance to us as we continue to advance our product candidates through research and development.

Legal Proceedings

We are not currently subject to any material legal proceedings.

Facilities

Our facilities consist of office space of approximately 7,125 square feet in Crestwood, Kentucky under a lease that expires in July 2018, office space of approximately 6,125 square feet in Waltham, Massachusetts under a lease that expires in June 2022, office space of approximately 1,250 square feet in Cambridge, Massachusetts under a lease that expires in October 2018, and office space of approximately 1,875 square feet in San Francisco, California under a lease that expires in June 2019.

Employees

As of February 28, 2018, we had 39 full-time or part-time employees, including three employees with M.D./Ph.D. degrees, two employees with M.D. degree and four employees with Ph.D. degrees. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider the relationship with our employees to be good.

MANAGEMENT

The following table sets forth the name, age as of the date of this prospectus and position of each of our executive officers and directors.

Name	Age	Position
Cedric Francois, M.D., Ph.D.	45	President, Chief Executive Officer and Director
Pascal Deschatelets, Ph.D.	48	Chief Operating Officer
Timothy Sullivan	47	Chief Financial Officer and Treasurer
Steven Axon	43	Chief Business Officer
Federico Grossi, M.D., Ph.D.	43	Executive Vice President of Clinical Development
Nicole Perry	53	Vice President Finance
Lukas Scheibler, Ph.D.	47	Executive Vice President of Research and Development
David Watson	45	General Counsel
Gerald Chan, D.Sc.(3)	67	Chairman of the Board of Directors
A. Sinclair Dunlop(1)(3)	46	Director
Alec Machiels(1)(2)	45	Director
Stephanie Monaghan O'Brien(1)(2)(3)	59	Director

(1) Member of the audit committee
(2) Member of the compensation committee
(3) Member of the nominating and corporate governance committee

Executive Officers

Cedric Francois, M.D., Ph.D., is a co-founder of our company and has served as a member of our board of directors and as our President and Chief Executive Officer since our inception. Prior to co-founding our company, Dr. Francois co-founded Potentia Pharmaceuticals, Inc., or Potentia, a private biotechnology company, the assets of which we purchased in September 2015. Dr. Francois has served as President and Chief Executive Officer at Potentia since 2001 and has served as a director of Potentia since 2003. Dr. Francois received his M.D. from the University of Leuven in Belgium and his Ph.D. in physiology from the University of Louisville. Following postgraduate training in pediatric and transplant surgery, Dr. Francois was a member of the research team that performed the first successful hand transplantation and of the Louisville Face Transplant Team, whose work supported hand transplantation in Lyon, France. We believe that Dr. Francois is qualified to serve on our board of directors because of his expertise and extensive leadership experience in immunology and immune system-mediated diseases and his extensive knowledge of our company based on his role as co-founder and Chief Executive Officer.

Pascal Deschatelets, Ph.D., is a co-founder of our company and has served as our Chief Operating Officer since our inception. Dr. Deschatelets also co-founded Potentia and served as its Chief Operating Officer from 2001 to September 2016. Dr. Deschatelets received his Ph.D. in organic chemistry from the University of Montreal and his post-doctoral training in the laboratory of Dr. George Whitesides at Harvard University.

Timothy Sullivan has served as our Chief Financial Officer and Treasurer since October 2017. From January 2014 to October 2017, Mr. Sullivan served as Partner at AJU IB Investment, a venture capital firm, at which he led the firm's investments in life sciences companies. Prior to joining AJU IB Investment, from December 2011 to January 2014, Mr. Sullivan was Managing Director, Head of Life Sciences at RBS Citizens. Mr. Sullivan was an observer on our board of directors from November 2014 until October 2017. Mr. Sullivan has previously served as a director of G1 Therapeutics, Inc. and Molecular Templates, Inc. Mr. Sullivan received his M.B.A. from the Columbia Business School and his B.A. in Biology from Harvard University.

Steven Axon has served as our Chief Business Officer since January 2017. From 2005 to July 2016, Mr. Axon served at Merck Serono in Geneva and Boston in leadership roles in Corporate Strategy, Alliance

Management and Business Development. Most recently, Mr. Axon served as Senior Vice President, Business Development with global responsibility for all late stage and commercial transactions. Prior to this, Mr. Axon was Global Head of Alliance Management with responsibility for over 40 strategic research and development collaborations. Prior to joining Merck Serono, Mr. Axon was Director of Strategy and Business Development at Serono in Geneva from 2005 until its acquisition by Merck KGaA in 2007. During the transition, Mr. Axon served as the Serono business lead for the Merck Serono integration. Mr. Axon received a B.Sc. and M.Sc. in biomechanical and biomedical engineering from the University of Toronto and his M.B.A. from the International Institute for Management Development in Lausanne, Switzerland.

Federico Grossi, M.D., Ph.D. has served as our Executive Vice President of Clinical Development since October 2017, having previously served as our Vice President of Clinical Development from October 2014 to October 2017 and as our Clinical Research Director from April 2010 to June 2012. Dr. Grossi served as Executive Vice President of Potentia from October 2013 to September 2014, and as Clinical Research Director of Potentia from 2006 to April 2010. From June 2012 to October 2014, Dr. Grossi worked as an independent early stage clinical research consultant. Dr. Grossi received his M.D. from the University of Córdoba in Argentina and his Ph.D. in physiology from the University of Louisville. Following his post-graduate training in surgery, where he developed his expertise in microsurgery and composite tissue transplantation, Dr. Grossi joined the Plastic Surgery Research Laboratory at the University of Louisville.

Nicole Perry has served as our Vice President of Finance since April 2015. From April 2015 to June 2015, Ms. Perry also served as Vice President of Finance at Revon Systems, LLC, or Revon, a private health care technology platform company. From August 2000 to April 2015, Ms. Perry worked as an independent consultant providing services to clients primarily in the areas of financial reporting, internal control compliance and as a liaison with external accountants, bankers and legal counsel. Prior to having her consulting practice, Ms. Perry worked in the audit practices of PricewaterhouseCoopers and Deloitte. Ms. Perry is a Certified Public Accountant and received her B.B.A. in accounting, with distinction, from the University of Oklahoma.

Lukas Scheibler, Ph.D. has served as our Executive Vice President of Research and Development since April 2018. From August 2015 to December 2017, Dr. Scheibler served as head of research and development and executive vice president at Acucela Inc., a biopharmaceutical company. From June 2008 until July 2015, he served in leadership roles in research and development at Alcon Laboratories, Inc., a subsidiary of Novartis AG focused on eye care products, including as vice president, head of ideation and technology evaluation center from October 2013 to July 2015 and as vice president, global head clinical trial management from October 2011 to October 2013. Dr. Scheibler received M.Sc. in chemistry from the University of Basel in Switzerland, a Ph.D. in chemistry from the University of Lausanne in Switzerland and completed his post-doctoral training at Harvard Medical School.

David Watson has served as our General Counsel and Vice President of Corporate Development since January 2014. From January 2014 to June 2015, Mr. Watson also served as General Counsel and Executive Vice President of Revon. From 2006 to December 2013, Mr. Watson was a member at the law firm Frost Brown Todd LLC, where his practice included equity finance, mergers and acquisitions and securities transactions. Mr. Watson received his B.A. from Harvard College, his J.D. from Vanderbilt Law School and his M.A. in mathematics from the University of Kentucky.

Non-Employee Directors

Gerald Chan, D.Sc. has served as a member of our board of directors and as Chairman since July 2013. Dr. Chan co-founded Morningside, a private investment group with venture, private equity and property investments, in 1986. He has served as a member of the Global Advisory Council of the International Society for Stem Cell Research since 2008, the Global Advisory Council of Harvard University since 2012, the Dean’s Board of Advisors of the Harvard School of Public Health since 2011, the advisory board of the Johns Hopkins Nanjing Center since 2004 and has chaired the Innovation Advisory Committee of Wellcome Trust since 2016.

Dr. Chan also has been a member of the board of directors of Hang Lung Group Limited since 1986, and Aduro Biotech Inc. since 2014. Dr. Chan received his B.S. and M.S. degrees in engineering from the University of California, Los Angeles, and his Master's degree in medical radiological physics and Doctor of Science degree in radiation biology from Harvard University. He did his post-doctoral training at the Dana-Farber Cancer Institute. Dr. Chan was elected to membership in the American Academy of Arts and Sciences in 2017. We believe that Dr. Chan is qualified to serve on our board of directors because of his extensive experience in life science investments and serving on boards of directors.

A. Sinclair Dunlop has served as a member of our board of directors since March 2010. Mr. Dunlop is a co-founder of venture capital fund Epidarex Capital, and has served as the Managing Partner since July 2010. Since 2005, Mr. Dunlop has served as the Managing Partner of venture capital fund Masa Life Science Ventures, LP. Mr. Dunlop currently serves on the board of directors of several private companies, including Potentia. Mr. Dunlop received his M.B.A. from Columbia Business School where he was the R.C. Kopf British-American Fellow in international business. He also received an M.A. with Honors in political economy from the University of Glasgow and an M.A. in international relations from the Maxwell School of Citizenship and Public Affairs at Syracuse University. We believe that Mr. Dunlop is qualified to serve on our board of directors because of his extensive investment and business experience.

Alec Machiels is a co-founder of our company and has served as a member of our board of directors since September 2009. Since 2006, Mr. Machiels has served as a Partner at Pegasus Capital Advisors, L.P., a private equity firm that he joined in 2002. Mr. Machiels is currently a director of Potentia, which he co-founded; Mr. Machiels serves on the board of directors of Creative Realities Inc. and the board of directors of several private companies. Mr. Machiels previously served on the board of directors of Molycorp, Inc. He started his career as a financial analyst in the Financial Services Group at Goldman Sachs International in London and in the Private Equity Group at Goldman, Sachs & Co. in New York from July 1996 until June 1999. Mr. Machiels received an M.B.A. from Harvard Business School in 2001. Mr. Machiels also received a license in law from KU Leuven Law School in Belgium and a masters in international economics from Konstanz University in Germany. We believe that Mr. Machiels is qualified to serve on our board of directors because of his strong background in financial management and investment in businesses and his experience serving on the boards of both public and private companies.

Stephanie Monaghan O'Brien has served as a member of our board of directors since July 2013. Ms. O'Brien has been a member of the investment team at Morningside since 1997. She has served as a director of Aduro Biotech Inc. since 2011, and as a director of numerous private nonclinical and clinical-stage companies developing drugs across a broad spectrum of therapeutic focus, including oncology and immunotherapy, and has extensive experience providing operational and management oversight to venture-backed technology companies. She has also facilitated multiple financings for public and private companies such as Dendreon Corporation, BioVex Group, Inc., Stealth Biotherapeutics Inc. and Sohu.com. Prior to joining Morningside, Ms. O'Brien spent nine years as a corporate lawyer with Hale and Dorr in its Boston and Washington, D.C. offices, working primarily on public offerings, venture capital finances and start-up companies. She previously worked at Chase Manhattan Bank, working in international portfolio analysis. She received her A.B., cum laude, from Harvard College and her J.D. from New York University School of Law. We believe that Ms. O'Brien is qualified to serve on our board of directors because of her strong background working with biotechnology companies and her extensive experience serving on the boards of both public and private companies.

Board Composition and Election of Directors

Board Composition

Our board of directors currently consists of five members. Our directors hold office until their successors have been elected and qualified or until the earlier of their resignation or removal. In accordance with the terms of our restated certificate of incorporation and amended and restated bylaws, our board of directors is divided

into three classes, class I, class II and class III, with members of each class serving staggered three-year terms. The members of the classes are as follows:

- the class I director is Stephanie Monaghan O'Brien, and her term expires at the annual meeting of stockholders to be held in 2018;
- the class II directors are A. Sinclair Dunlop and Alec Machiels, and their term expires at the annual meeting of stockholders to be held in 2019; and
- the class III directors are Gerald Chan and Cedric Francois, and their term expires at the annual meeting of stockholders to be held in 2020.

Our restated certificate of incorporation and amended and restated bylaws provide that the authorized number of directors may be changed only by resolution of our board of directors. Our restated certificate of incorporation and amended and restated bylaws also provide that our directors may be removed only for cause by the affirmative vote of the holders of 75% of our shares of capital stock present in person or by proxy and entitled to vote, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

Director Independence

Applicable rules of The Nasdaq Stock Market LLC, or Nasdaq, require a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, the Nasdaq rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and compensation committee members must also satisfy the independence criteria set forth in Rule 10C-1 under the Exchange Act. Under applicable Nasdaq rules, a director will only qualify as an "independent director" if, in the opinion of the listed company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries. In order to be considered independent for purposes of Rule 10C-1 under the Exchange Act, the board must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: the source of compensation of the director, including any consulting advisory or other compensatory fee paid by such company to the director, and whether the director is affiliated with the company or any of its subsidiaries or affiliates.

In March 2018, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that each of our directors, with the exception of Cedric Francois, is an "independent director" as defined under applicable Nasdaq rules, including, in the case of all the members of our audit committee, the independence criteria set forth in Rule 10A-3 under the Exchange Act, and in the case of all the members of our compensation committee, the independence criteria set forth in Rule 10C-1 under the Exchange Act. In making such determination, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances that our board of directors deemed relevant in determining his or her independence, including the beneficial ownership of our capital stock by each non-employee director. Dr. Francois is not deemed to be an independent director under these rules because he is our President and Chief Executive Officer.

There are no family relationships among any of our directors or executive officers, other than Drs. Francois and Grossi, who are brothers-in-law.

Board Committees

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee. Each of these committees operates under a charter that has been approved by our board of directors.

Audit Committee

The members of our audit committee are Alec Machiels, A. Sinclair Dunlop and Stephanie Monaghan O'Brien, and Mr. Machiels is the chair of the audit committee. Our audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of reports from that firm;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- overseeing our internal audit function, if any;
- overseeing our risk assessment and risk management policies;
- establishing procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with our internal auditing staff, if any, our independent registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by Securities and Exchange Commission, or SEC, rules.

All audit and non-audit services, other than *de minimis* non-audit services, to be provided to us by our independent registered public accounting firm must be approved in advance by our audit committee.

Our board of directors has determined that Mr. Machiels is an "audit committee financial expert" as defined in applicable SEC rules and that each of the members of our audit committee possesses the financial sophistication required for audit committee members under Nasdaq rules. We believe that the composition of our audit committee meets the requirements for independence under current Nasdaq and SEC rules and regulations.

Compensation Committee

The members of our compensation committee are Stephanie Monaghan O'Brien and Alec Machiels, and Ms. O'Brien is the chair of the compensation committee. Our compensation committee's responsibilities include:

- reviewing and approving, or making recommendations to our board of directors with respect to, the compensation of our Chief Executive Officer and our other executive officers;
- overseeing an evaluation of our senior executives;
- overseeing and administering our cash and equity incentive plans;

- reviewing and making recommendations to our board of directors with respect to director compensation and management succession planning;
- reviewing and discussing annually with management our "Compensation Discussion and Analysis" disclosure if and to the extent then required by SEC rules; and
- preparing the compensation committee report if and to the extent then required by SEC rules.

We believe that the composition of our compensation committee meets the requirements for independence under current Nasdaq and SEC rules and regulations.

Nominating and Corporate Governance Committee

The members of our nominating and corporate governance committee are Gerald Chan, A. Sinclair Dunlop and Stephanie Monaghan O'Brien, and Dr. Chan is the chair of the nominating and corporate governance committee. Our nominating and corporate governance committee's responsibilities include:

- identifying individuals qualified to become members of our board of directors;
- recommending to our board of directors the persons to be nominated for election as directors and to each of our board's committees;
- reviewing and making recommendations to our board of directors with respect to our board leadership structure and board committee structure;
- developing and recommending corporate governance guidelines to our board of directors; and
- overseeing an annual evaluation of our board of directors.

We believe that the composition of our nominating and corporate governance committee meets the requirements for independence under current Nasdaq and SEC rules and regulations.

Compensation Committee Interlocks and Insider Participation

None of our executive officers serves, or in the past year has served, as a member of the board of directors or compensation committee, or other committee serving an equivalent function, of any other entity that has one or more of its executive officers serving as a member of our board of directors or our compensation committee. None of the members of our compensation committee is, or has ever been, an officer or employee of our company.

Code of Business Conduct and Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer principal accounting officer or controller, or persons performing similar functions. This code is available on our website, which is located at *www.apellis.com*. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

EXECUTIVE COMPENSATION

This section describes the material elements of compensation awarded to, earned by or paid to each of our named executive officers in 2017. Our named executive officers for 2017 were Cedric Francois, Pascal Deschatelets and Timothy Sullivan. This section also provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our executive officers and is intended to place in perspective the data presented in the tables and narrative that follow.

Summary Compensation Table

The following table sets forth information regarding compensation awarded to, earned by or paid to our named executive officers during 2017 and 2016.

Name and principal position	Year	Salary ($)	Bonus ($)(1)	Option Awards ($)(2)	Total ($)
Cedric Francois, M.D., Ph.D.(3)	2017	400,000	225,000	1,037,972	1,663,422
President and Chief Executive Officer	2016	325,000	290,000	882,511	1,497,511
Pascal Deschatelets, Ph.D.	2017	279,227	120,000	461,321	860,998
Chief Operating Officer	2016	250,000	135,000	567,737	952,737
Timothy Sullivan(4)	2017	68,939	40,000	2,187,760	2,296,699
Chief Financial Officer					

(1) The amounts reported in the “Bonus” column represent discretionary annual cash bonuses awarded to our named executive officers.
(2) The amounts reported in the “Options Awards” column reflect the aggregate grant date fair value of share-based compensation awarded during the year computed in accordance with the provisions of Financial Accounting Standards Board Accounting Standards Codification, or ASC, Topic 718.
(3) Dr. Francois also serves as a member of our board of directors but does not receive any additional compensation for his service as a director.
(4) Mr. Sullivan joined Apellis as our Chief Financial Officer in October 2017. The salary information for 2017 reflects the pro-rated portion of Mr. Sullivan’s annual salary of $325,000 attributable to the portion of the year during which he served as our Chief Financial Officer.

Narrative to Summary Compensation Table

In 2017, we paid annual base salaries of $400,000 to Dr. Francois, $279,227 to Dr. Deschatelets and $68,939 to Mr. Sullivan. We use base salaries to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. None of our named executive officers is currently party to an employment agreement or other agreement or arrangement that provides for automatic or scheduled increases in base salary. In March 2018, our board of directors approved annual base salaries for 2018 of $555,000 for Dr. Francois, $400,000 for Dr. Deschatelets and $380,000 for Mr. Sullivan.

We do not have a formal performance-based bonus plan. From time to time, our board of directors has approved discretionary annual cash bonuses to our named executive officers with respect to their prior year performance. In addition, under the terms of the offer letter we entered into with Mr. Sullivan, he was eligible for a discretionary annual bonus of up to 20% of his annualized base salary in 2017. In December 2017, Dr. Francois, Dr. Deschatelets and Mr. Sullivan received cash bonuses of $225,000, $120,000 and $40,000, respectively, for services performed during 2017. In March 2018, our board of directors established target bonuses as a percentage of annual base salary for 2018 of 55% for Dr. Francois, 45% for Dr. Deschatelets and 40% for Mr. Sullivan.

Although we do not have a formal policy with respect to the grant of equity incentive awards to our executive officers, or any formal equity ownership guidelines applicable to them, we believe that equity grants provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our stockholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incents our executive officers to remain in our employment during the vesting period. Accordingly, our board of directors periodically reviews the equity incentive compensation of our named executive officers and from time to time may grant equity incentive awards to them in the form of stock options.

In August 2017, our board of directors granted options to purchase 421,940 and 187,529 shares of common stock to Dr. Francois and Dr. Deschatelets, respectively, at an exercise price equal to $4.31 per share. Each of these options will vest as to 25% of the shares on August 21, 2018 and with respect to the remaining shares in approximately equal monthly installments through the fourth anniversary of the grant, subject to continued service.

In October 2017, in connection with his appointment as the Chief Financial Officer of our company, our board of directors granted to Mr. Sullivan options to purchase 398,499 shares of our common stock with an exercise price equal to $10.03 per share. This option grant will vest as to 25% of the shares on October 18, 2018 and with respect to the remaining shares in approximately equal monthly installments through the fourth anniversary of the grant, subject to continued service.

In February 2018, our board of directors granted options to purchase 280,000, 110,000 and 25,000 shares of common stock to Dr. Francois, Dr. Deschatelets and Mr. Sullivan, respectively, at an exercise price equal to $14.95 per share. Each of these options vests with respect to 25% of the shares on February 16, 2019 and with respect to the remaining shares in approximately equal monthly installments through the fourth anniversary of the grant, subject to continued service.

We do not provide perquisites or personal benefits to our named executive officers. We do, however, pay the premiums for life and medical insurance for all of our employees, including our named executive officers.

Outstanding Equity Awards at Fiscal Year End

The following table sets forth information regarding outstanding equity awards held by our named executive officers as of December 31, 2017, which consisted entirely of stock options:

	Option Awards			
Name	Number of Securities Underlying Unexercised Options Exercisable (#)	Number of Securities Underlying Unexercised Options Unexercisable (#)	Option Exercise Price ($/share)	Option Expiration Date
Cedric Francois, M.D., Ph.D.	—	421,940(1)	$ 4.31	8/20/27
	162,078	191,547(2)	$ 3.76	2/7/26
	515,705	—	$ 2.67	12/4/23
	468,823	—	$ 2.14	5/12/20
Pascal Deschatelets, Ph.D.	—	187,529(1)	$ 4.31	8/20/27
	104,268	123,226(2)	$ 3.76	2/7/26
	398,499	—	$ 2.67	12/4/23
	234,411	—	$ 2.14	5/12/20
Timothy Sullivan	—	398,499(3)	$ 10.03	10/17/27

(1) Granted on August 21, 2017. This option grant will vest as to 25% of the shares underlying the option on August 21, 2018. The remaining 75% of the shares underlying the option will vest in equal monthly

installments thereafter through August 21, 2021, subject to continued service. All shares subject to vesting under this option grant will vest in full and become immediately exercisable upon the closing of a change in control of our company.

(2) Granted on February 8, 2016. This option grant vested as to 25% of the shares underlying the option on February 8, 2017. The remaining 75% of the shares underlying the option will vest in equal monthly installments thereafter through February 8, 2020, subject to continued service. All shares subject to vesting under this option grant will vest in full and become immediately exercisable upon the closing of a change in control of our company.

(3) Granted on October 18, 2017. This option grant will vest as to 25% of the shares underlying the option on October 18, 2018. The remaining 75% of the shares underlying the option will vest in equal monthly installments thereafter through October 18, 2021, subject to continued service. All shares subject to vesting under this option grant will vest in full and become immediately exercisable upon the closing of a change in control of our company.

Employment and Change in Control Arrangements

We do not currently have employment agreements with Dr. Francois or Dr. Deschatelets, although we may enter into such agreements in the future.

In October 2017, we entered into an offer letter with Mr. Sullivan in connection with his appointment as the Chief Financial Officer of our company. Under the offer letter, Mr. Sullivan is an at will employee, and his employment with us can be terminated by him or us at any time and for any reason. Prior to adjustments made by our board of directors in March 2018, Mr. Sullivan's offer letter provided for an annual base salary of $325,000 and a discretionary annual bonus of up to 20% of his annualized base salary.

Under our 2010 equity incentive plan, as amended to date, or the 2010 plan, upon a change in control (as defined in the 2010 plan) any outstanding awards then held by a named executive officer which are unexercisable or otherwise unvested or subject to lapse restrictions will automatically be deemed exercisable or vested or no longer subject to lapse restrictions (as the case may be). We do not have any other agreements with our named executive officers that provide for payments upon termination, retirement or in connection with a change in control of the company.

Stock Option and Other Compensation Plans

The equity incentive plans described in this section are our 2017 stock incentive plan, or the 2017 plan, our 2017 employee stock purchase plan, or the 2017 ESPP, and our 2010 plan. Prior to our initial public offering, we granted awards to eligible participants under the 2010 plan. Following the effectiveness of the registration statement for our initial public offering, we ceased granting awards under the 2010 plan and started granting awards to eligible participants only under the 2017 plan.

2017 Stock Incentive Plan

Our 2017 plan, which became effective on November 8, 2017, was adopted by our board of directors and approved by our stockholders in October 2017. The 2017 plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, awards of restricted stock, restricted stock units and other stock-based awards. The number of shares of our common stock reserved for issuance under the 2017 plan is the sum of (i) 3,742,844 shares plus (ii) the number of shares of our common stock subject to outstanding awards under our 2010 plan upon effectiveness of the 2017 plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by us at their original issuance price pursuant to a contractual repurchase right plus (iii) an annual increase, to be added the first day of each fiscal year continuing until, and including, the fiscal year ending December 31, 2027, equal to the lowest of 4,219,409 shares of our common stock, 4.0% of the number of shares of our common stock outstanding on the first day of the fiscal year and an amount determined

by our board of directors. Our employees, officers, directors, consultants and advisors are eligible to receive awards under the 2017 plan; however, incentive stock options may only be granted to our employees.

As of December 31, 2017, there were options to purchase 537,737 shares of our common stock outstanding under the 2017 plan, at a weighted-average exercise price of $14.00 per share, and no options to purchase shares of our common stock had been exercised. Since December 31, 2017, we have granted additional options to purchase an aggregate of 1,126,585 shares of our common stock under our 2017 plan, at a weighted-average exercise price of $15.13. On January 1, 2018, pursuant to the terms of the 2017 plan, an additional 2,013,366 shares were reserved for issuance under the 2017 plan. As of February 28, 2018, a total of 2,078,522 shares remain available for issuance under the 2017 plan.

Pursuant to the terms of the 2017 plan, our board of directors (or a committee delegated by our board of directors) administers the 2017 plan and, subject to any limitations set forth in the 2017 plan, will select the recipients of awards and determine:

- the number of shares of common stock covered by options and the dates upon which those options become exercisable;
- the type of options to be granted;
- the exercise price of options, which price must be at least equal to the fair market value of our common stock on the date of grant;
- the duration of options, which may not be in excess of ten years;
- the methods of payment of the exercise price of options; and
- the number of shares of our common stock subject to, and the terms of, any stock appreciation rights, awards of restricted stock, restricted stock units or other stock-based awards, including the issue price, conditions for repurchase, repurchase price and performance conditions (though the measurement price of stock appreciation rights must be at least equal to the fair market value of our common stock on the date of grant and the duration of such awards may not be in excess of ten years), if any.

If our board of directors delegates authority to an executive officer to grant awards under the 2017 plan, the executive officer will have the power to make awards to all of our employees, except executive officers. Our board of directors will fix the terms of the awards to be granted by such executive officer, including the exercise price of such awards (or a formula for establishing such price), and the maximum number of shares subject to awards that such executive officer may make.

In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend, we are required by the 2017 plan to make equitable adjustments (or make substitute awards, if applicable), in a manner determined by our board, to:

- the number and class of securities available under the 2017 plan;
- the share counting rules under the 2017 plan;
- the number and class of securities and exercise price per share of each outstanding option;
- the share and per-share provisions and measurement price of each outstanding stock appreciation right;
- the number of shares and the repurchase price per share subject to each outstanding restricted stock award or restricted stock unit award; and
- the share and per-share related provisions and purchase price, if any, of any outstanding other stock-based award.

Upon a merger or other reorganization event (as defined in our 2017 plan), our board of directors, may, on such terms as our board determines (except to the extent specifically provided otherwise in an applicable award agreement or other agreement between the participant and us), take any one or more of the following actions pursuant to the 2017 plan, as to some or all outstanding awards, other than restricted stock awards:

- provide that all outstanding awards will be assumed or substantially equivalent awards will be substituted by the successor corporation (or an affiliate thereof);
- upon written notice to a participant, provide that the participant's unvested and/or unexercised options or other awards will terminate immediately prior to the consummation of such transaction unless exercised by the participant;
- provide that outstanding awards will become exercisable, realizable or deliverable, or restrictions applicable to an award will lapse, in whole or in part, prior to or upon the reorganization event;
- in the event of a reorganization event pursuant to which holders of our common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to the participants with respect to each award held by a participant equal to (1) the number of shares of our common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (2) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of such award;
- provide that, in connection with a liquidation or dissolution, awards convert into the right to receive liquidation proceeds (if applicable, net of exercise, measurement or purchase price thereof and any applicable tax withholdings); or
- any combination of the foregoing.

Our board of directors is not obligated by the 2017 plan to treat all awards, all awards held by a participant, or all awards of the same type, identically.

In the case of certain restricted stock units, no assumption or substitution is permitted, and the restricted stock units will instead be settled in accordance with the terms of the applicable restricted stock unit agreement.

Upon the occurrence of a reorganization event other than a liquidation or dissolution, the repurchase and other rights under each outstanding restricted stock award will continue for the benefit of the successor company and will, unless our board of directors may otherwise determine, apply to the cash, securities or other property which our common stock is converted into or exchanged for pursuant to the reorganization event, unless our board provided for the termination or deemed satisfaction of such repurchase or other rights under the restricted stock award agreement or any other agreement between the participant and us. Upon the occurrence of a reorganization event involving a liquidation or dissolution, all restrictions and conditions on each outstanding restricted stock award will automatically be deemed terminated or satisfied, unless otherwise provided in the agreement evidencing the restricted stock award or in any other agreement between the participant and us.

Our board of directors may at any time provide that any award under the 2017 plan shall become immediately exercisable in whole or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part, as the case may be.

Except with respect to certain actions requiring stockholder approval under the Internal Revenue Code or Nasdaq rules, our board of directors may amend, modify or terminate any outstanding award under the 2017 plan, including but not limited to, substituting therefor another award of the same or a different type, changing the date of exercise or realization, and converting an incentive stock option into a nonstatutory stock option, subject to certain participant consent requirements. Unless our stockholders approve such action, the 2017 plan

provides that we may not (except as otherwise permitted in connection with a change in capitalization or reorganization event):

- amend any outstanding stock option or stock appreciation right granted under the 2017 plan to provide an exercise or measurement price per share that is lower than the then-current exercise or measurement price per share of such outstanding award;
- cancel any outstanding option or stock appreciation right (whether or not granted under the 2017 plan) and grant in substitution therefor new awards under the 2017 plan (other than substitute awards permitted in connection with a merger or consolidation of an entity with us or our acquisition of property or stock of another entity) covering the same or a different number of shares of our common stock and having an exercise or measurement price per share lower than the then-current exercise or measurement price per share of the cancelled award;
- cancel in exchange for a cash payment any outstanding option or stock appreciation right with an exercise or measurement price per share above the then-current fair market value of our common stock; or
- take any other action that constitutes a "repricing" within the meaning of the Nasdaq rules.

No award may be granted under the 2017 plan on or after November 8, 2027. Our board of directors may amend, suspend or terminate the 2017 plan at any time, except that stockholder approval will be required to comply with applicable law or stock market requirements.

2010 Equity Incentive Plan

Our 2010 plan was adopted by our board of directors in May 2010 and approved by our stockholders in December 2010. An amendment to the 2010 plan to increase the number of shares underlying the 2010 plan from 1,172,058 shares to 2,437,880 shares was adopted by our board of directors in July 2013, and approved by our stockholders in July 2013. A second amendment to the 2010 plan to increase the number of shares underlying the 2010 plan from 2,437,880 shares to 3,375,527 shares was adopted by our board of directors, and approved by our stockholders, in November 2014. A third amendment to the 2010 plan to provide the compensation committee with the ability to vest awards at the time of a change of control was adopted by our board of directors in February 2016. A fourth amendment to the 2010 plan to increase the number of shares underlying the 2010 plan from 3,375,527 shares to 4,781,997 shares was adopted by our board of directors in June 2016, and approved by our stockholders, in September 2016. A fifth amendment to the 2010 plan to increase the number of shares underlying the 2010 plan from 4,781,997 shares to 6,188,466 shares was adopted by our board of directors and approved by our stockholders in August 2017. Our 2010 plan provided for the grant of incentive stock options, nonqualified stock options, restricted stock awards, stock appreciation rights, performance share awards, performance stock units, dividend equivalents, stock payments, deferred stock, restricted stock units, other stock-based awards and performance bonus awards. Our employees, directors, and consultants were eligible to receive awards under our 2010 plan; however, incentive stock options could only be granted to our employees. Our board of directors (or a committee delegated by our board of directors) administers the 2010 plan.

Our board of directors may terminate, amend or modify the 2010 plan at any time, except that stockholder approval may be required to comply with applicable law or stock market requirements.

In the event of any change in the outstanding shares of our stock by reason of any stock dividend or split, reorganization, recapitalization, merger, consolidation, spin-off, combination or transaction or exchange of shares of stock or other corporate exchange, or any distribution to our stockholders of shares of stock or cash other than regular cash dividends or any transaction similar to the foregoing, we shall make such substitution or adjustment, if any, as our board of directors deems to be equitable, as to:

- the number and kind of shares of stock or other securities issued or reserved for issuance pursuant to the 2010 plan or pursuant to outstanding awards;

- the maximum number of shares of stock for which options or stock appreciation rights may be granted during a calendar year to any participant in the 2010 plan;
- the maximum amount of a performance-based award that may be granted during a calendar year to any participant;
- the exercise price of any option or stock appreciation right; and
- any other affected terms of such awards under the 2010 plan.

Immediately prior to any change of control, as defined in the 2010 plan, or at such earlier date as provided thereunder, any outstanding awards then held by participants which are unexercisable or otherwise unvested or subject to lapse restrictions shall automatically be deemed exercisable or vested or no longer subject to lapse restrictions (as the case may be). In addition, prior to such change of control, the board of directors shall take one of the following actions with respect to each award issued under the 2010 plan:

- provide for the termination of such award in exchange for a cash payment equal to the fair value thereof (as determined in the sole discretion of the board of directors and pursuant to the terms of the 2010 plan);
- provide that such award shall be canceled and the participant shall receive in substitution therefor similar fully vested options, rights or awards covering the stock of the successor or surviving or acquiring entity, or a parent or subsidiary thereof, with appropriate adjustments as to the number and kind of shares and prices;
- provide, with respect to any award that must be exercised to obtain the benefits thereunder, that for a period of at least fifteen days prior to the change of control, such award shall be exercisable as to all shares of stock subject thereto and that upon the occurrence of the change of control, such award shall terminate and be of no further force and effect; or
- if the change of control occurs and our company is the surviving entity in a reorganization, merger or consolidation, to specify that the award, now fully vested and exercisable, shall remain outstanding upon the other terms stated in the applicable award agreement.

Our board of directors is not obligated by the 2010 plan to treat all awards, all awards held by a participant, or all awards of the same type, identically. In addition, the board may, in its sole discretion, accelerate the exercisability of any award or waive the forfeiture thereof, except in the case of performance-based awards.

In January 2016, our board of directors approved the repricing of 93,762 stock options that had exercise prices between $6.81 and $6.89 per share, to the estimated fair value of common stock, determined to be an exercise price of $3.76 per share. We repriced these options to align stock option exercise prices with the fair market value of common stock at that time and maintain our equity awards as an important retention tool for our key employees.

As of February 28, 2018, there were options to purchase 5,732,532 shares of our common stock outstanding under the 2010 plan, at a weighted-average exercise price of $3.89 per share, and options to purchase 47,613 shares of our common stock had been exercised. We no longer grant stock options or other awards under the 2010 plan. However, any shares of common stock subject to awards under our 2010 plan that expire, terminate, or are otherwise surrendered, canceled, forfeited or repurchased without having been fully exercised or resulting in any common stock being issued will become available for issuance under our 2017 plan.

2017 Employee Stock Purchase Plan

Our 2017 ESPP, which became effective on November 8, 2017, was adopted by our board of directors and approved by our stockholders in October 2017. The 2017 ESPP is administered by our board of directors or by a committee appointed by our board of directors. The 2017 ESPP will provide participating employees with the

opportunity to purchase up to an aggregate of 972,164 shares of our common stock. The number of shares of our common stock reserved for issuance under the 2017 ESPP will automatically increase on the first day of each fiscal year, continuing until, and including, the fiscal year ending December 31, 2027, equal to the lowest of (i) 937,646 shares of our common stock, (ii) 1.0% of the number of shares of our common stock outstanding on the first day of the fiscal year and (iii) an amount determined by our board of directors. On January 1, 2018, pursuant to the terms of the 2017 ESPP, an additional 503,341 shares were reserved for issuance under the 2017 ESPP.

All of our employees or employees of any designated subsidiary, as defined in the 2017 ESPP, are eligible to participate in the 2017 ESPP, provided that:

- such person is customarily employed by us or a designated subsidiary for more than 20 hours a week and for more than six months in a calendar year;
- such person has been employed by us or by a designated subsidiary for at least three months prior to enrolling in the 2017 ESPP; and
- such person was our employee or an employee of a designated subsidiary on the first day of the applicable offering period under the 2017 ESPP.

No employee may purchase shares of our common stock under the 2017 ESPP and any of our other employee stock purchase plans in excess of $25,000 of the fair market value of our common stock (as of the date of the option grant) in any calendar year. In addition, no employee may purchase shares of our common stock under the 2017 ESPP that would result in the employee owning 5% or more of the total combined voting power or value of our stock.

We expect to make one or more offerings to our eligible employees to purchase stock under the 2017 ESPP beginning at such time as our board of directors may determine. Each offering will consist of a six-month offering period during which payroll deductions will be made and held for the purchase of our common stock at the end of the offering period. Our board of directors may, at its discretion, choose a different period of not more than 12 months for offerings.

On the commencement date of each offering period, each eligible employee may authorize up to a maximum of 15% of his or her compensation to be deducted by us during the offering period. Each employee who continues to be a participant in the 2017 ESPP on the last business day of the offering period will be deemed to have exercised an option to purchase from us the number of whole shares of our common stock that his or her accumulated payroll deductions on such date will pay for, not in excess of the maximum numbers set forth above. Under the terms of the 2017 ESPP, the purchase price shall be determined by our board of directors for each offering period and will be at least 85% of the applicable closing price of our common stock. If our board of directors does not make a determination of the purchase price, the purchase price will be 85% of the lesser of the closing price of our common stock on the first business day of the offering period or on the last business day of the offering period.

An employee may for any reason withdraw from participation in an offering prior to the end of an offering period and permanently draw out the balance accumulated in the employee's account. If an employee elects to discontinue his or her payroll deductions during an offering period but does not elect to withdraw his or her funds, funds previously deducted will be applied to the purchase of common stock at the end of the offering period. If a participating employee's employment ends before the last business day of an offering period, no additional payroll deductions will be made and the balance in the employee's account will be paid to the employee.

We will be required to make equitable adjustments to the number and class of securities available under the 2017 ESPP, the share limitations under the 2017 ESPP, and the purchase price for an offering period under the 2017 ESPP to reflect stock splits, reverse stock splits, stock dividends, recapitalizations, combinations of shares, reclassifications of shares, spin-offs and other similar changes in capitalization or events or any dividends or distributions to holders of our common stock other than ordinary cash dividends.

In connection with a merger or other reorganization event, as defined in the 2017 ESPP, our board of directors or a committee of our board of directors may take any one or more of the following actions as to outstanding options to purchase shares of our common stock under the 2017 ESPP on such terms as our board or committee determines:

- provide that options shall be assumed, or substantially equivalent options shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);
- upon written notice to employees, provide that all outstanding options will be terminated immediately prior to the consummation of such reorganization event and that all such outstanding options will become exercisable to the extent of accumulated payroll deductions as of a date specified by our board or committee in such notice, which date shall not be less than ten days preceding the effective date of the reorganization event;
- upon written notice to employees, provide that all outstanding options will be cancelled as of a date prior to the effective date of the reorganization event and that all accumulated payroll deductions will be returned to participating employees on such date;
- in the event of a reorganization event under the terms of which holders of our common stock will receive upon consummation thereof a cash payment for each share surrendered in the reorganization event, change the last day of the offering period to be the date of the consummation of the reorganization event and make or provide for a cash payment to each employee equal to (1) the cash payment for each share surrendered in the reorganization event times the number of shares of our common stock that the employee's accumulated payroll deductions as of immediately prior to the reorganization event could purchase at the applicable purchase price, where the acquisition price is treated as the fair market value of our common stock on the last day of the applicable offering period for purposes of determining the purchase price and where the number of shares that could be purchased is subject to the applicable limitations under the 2017 ESPP minus (2) the result of multiplying such number of shares by the purchase price; and/or
- provide that, in connection with our liquidation or dissolution, options shall convert into the right to receive liquidation proceeds (net of the purchase price thereof).

Our board of directors may at any time, and from time to time, amend or suspend the 2017 ESPP or any portion thereof. We will obtain stockholder approval for any amendment if such approval is required by Section 423 of the Internal Revenue Code. Further, our board of directors may not make any amendment that would cause the 2017 ESPP to fail to comply with Section 423 of the Internal Revenue Code. The 2017 ESPP may be terminated at any time by our board of directors. Upon termination, we will refund all amounts in the accounts of participating employees.

401(k) Retirement Plan

We maintain a 401(k) retirement plan that is intended to be a tax-qualified defined contribution plan under Section 401(k) of the Code. In general, all of our full-time employees are eligible to participate, beginning on the first day of the month following commencement of their employment. The 401(k) plan includes a salary deferral arrangement pursuant to which participants may elect to reduce their current compensation by up to the statutorily prescribed limit, equal to $18,500 in 2018, and have the amount of the reduction contributed to the 401(k) plan.

Limitations on Liability and Indemnification

Our restated certificate of incorporation limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the General Corporation Law of the State of Delaware and provides that no director will have personal liability to us or to our stockholders for monetary damages for breach of fiduciary

duty or other duty as a director. However, these provisions do not eliminate or limit the liability of any of our directors:

- for any breach of the director's duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- for voting for or assenting to unlawful payments of dividends, stock repurchases or other distributions; or
- for any transaction from which the director derived an improper personal benefit.

Any amendment to or repeal of these provisions will not eliminate or reduce the effect of these provisions in respect of any act, omission or claim that occurred or arose prior to such amendment or repeal. If the General Corporation Law of the State of Delaware is amended to provide for further limitations on the personal liability of directors of corporations, then the personal liability of our directors will be further limited to the greatest extent permitted by the General Corporation Law of the State of Delaware.

In addition, our restated certificate of incorporation provides that we must indemnify our directors and officers and we must advance expenses, including attorneys' fees, to our directors and officers in connection with legal proceedings, subject to very limited exceptions.

We maintain a general liability insurance policy that covers specified liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers. In addition, we have entered into indemnification agreements with all of our directors and executive officers. These indemnification agreements may require us, among other things, to indemnify each such director or officer for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by him or her in any action or proceeding arising out of his or her service as one of our directors or officers.

Some of our non-employee directors may, through their relationships with their employers, be insured or indemnified against specified liabilities incurred in their capacities as members of our board of directors.

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, or the Securities Act, may be permitted to directors, executive officers or persons controlling us, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Rule 10b5-1 Trading Plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without subsequent direction from the director or officer. The director or officer may amend or terminate the plan in some circumstances. Our directors and executive officers may also buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

Director Compensation

The following table sets forth information regarding compensation earned by our non-employee directors during 2017.

Name	Fees Earned or Paid in Cash ($)(1)	Option Awards ($)(2)	Total ($)
Gerald Chan, D.Sc.	10,514	810,595	821,109
A. Sinclair Dunlop	7,489	810,595	818,084
Alec Machiels	8,785	810,595	819,380
Stephanie Monaghan O'Brien	8,929	810,595	819,524

(1) Amounts represent cash compensation for services rendered by each member of the board of directors.
(2) In 2017, each of Dr. Chan, Mr. Dunlop, Mr. Machiels and Ms. O'Brien was granted an option to purchase 121,894 shares of our common stock under the 2017 Plan.
(3) The amounts reported in the "Option Awards" column reflect the aggregate grant date fair value of stock-based compensation awarded during the year computed in accordance with the provisions of ASC Topic 718.

Robert Adelman, M.D., Bihua Chen and Maha Katabi, Ph.D. were members of our board of directors until their voluntary resignation from our board of directors in November 2017 in connection with our initial public offering. Neither Dr. Adelman, Ms. Chen nor Dr. Katabi earned any compensation from us for their service a director in 2017.

We do not pay any compensation to our President and Chief Executive Officer in connection with his service on our board of directors. The compensation that we pay to our President and Chief Executive Officer is discussed earlier in this "Executive Compensation" section.

Director Compensation Program

Prior to November 2017, we did not pay cash compensation to any non-employee director for his or her service as a director. In October 2017, our board of directors approved a director compensation program that became effective at the time of our initial public offering in November 2017. This program is intended to provide a total compensation package that enables us to attract and retain qualified and experienced individuals to serve as directors and to align our directors' interests with those of our stockholders.

Under our director compensation program, we pay our non-employee directors a cash retainer for service on the board of directors and for service on each committee on which the director is a member. The chairman of each committee and the chairman of the board of directors receive higher retainers for such service. These fees are payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment is prorated for any portion of such quarter that the director is not serving on our board of directors, on such committee or in such position. The fees paid to non-employee directors for service on the board of directors and for service on each committee of the board of directors on which the director is a member are as follows:

	Member Annual Fee ($)	Chairman Additional Annual Fee ($)
Board of Directors	40,000	25,000
Audit Committee	8,000	8,000
Compensation Committee	5,000	5,000
Nominating and Corporate Governance Committee	4,000	4,000

We also reimburse our non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending our board of director and committee meetings.

In addition, under our director compensation program, on November 8, 2017, each non-employee director received options to purchase 121,894 shares of our common stock under the 2017 plan. Each of these options vested with respect to 50% of such options immediately upon grant, and will vest with respect to the balance of the options in 12 equal monthly installments with the first installment vesting on December 8, 2017, subject to the non-employee director's continued service as a director. Each non-employee director that may be elected to our board of directors in the future will receive an option to purchase 35,161 shares of our common stock upon his or her initial election to the board of directors. Each of these options will vest with respect to one-third of the award on each of the first, second and third anniversaries of the grant date, subject to the non-employee director's continued service as a director.

Further, on January 1st of each year, beginning on January 1, 2019, each non-employee director that has served on our board of directors for at least six months will receive an option to purchase 17,580 shares of our common stock. Each of these options will vest in four equal quarterly installments on April 1, July 1 and October 1 of the year in which the grant is made and on January 1 of the following year, unless otherwise provided at the time of grant, subject to the non-employee director's continued service as a director. All options issued to our non-employee directors under our director compensation program will become exercisable in full upon a change in control of our company, will be granted at an exercise price per share equal to the fair market value of our common stock on the date of grant, and will have a term of ten years.

Prior to our initial public offering, other than an option to purchase 187,529 shares of our common stock, at an exercise price of $2.67 per share, which was granted to Mr. Machiels in 2013 for his service as a director, we did not pay cash retainers or other compensation with respect to service on our board of directors. We have historically reimbursed our directors for reasonable travel and out-of-pocket expenses incurred in connection with attending board of director and committee meetings.

Director Equity Outstanding at 2017 Fiscal Year End

As of December 31, 2017, our non-employee directors held the following stock options, all of which were granted under our 2010 plan or 2017 plan:

Name	Option Awards
Gerald Chan, D.Sc.	121,894
A. Sinclair Dunlop	121,894
Alec Machiels	309,423
Stephanie Monaghan O'Brien	121,894

TRANSACTIONS WITH RELATED PERSONS

Since January 1, 2015, we have engaged in the following transactions in which the amount involved exceeded $120,000 and any of our directors or executive officers or beneficial holders of more than 5% of any class of our voting securities, or any immediate family member of the foregoing persons, had a material interest. We believe that all of these transactions were on terms comparable to terms that could have been obtained from unrelated third parties.

Series C Convertible Preferred Stock Financings

In closings that occurred in December 2014, January 2015, March 2015 and May 2015, we issued and sold an aggregate of 11,821,432 shares of our series C convertible preferred stock at a price per share of $1.50, for an aggregate purchase price of $17.7 million. The following table sets forth the number of shares of our series C convertible preferred stock purchased in these closings by our 5% stockholders at the time of the transactions and their affiliates and the aggregate purchase price paid for such shares. Upon the closing of our initial public offering, all of the outstanding shares of our series C convertible preferred stock converted into shares of our common stock.

Name	Shares of Series C Convertible Preferred Stock Purchased	Aggregate Purchase Price
Morningside Venture Investments, Ltd.(1)(2)	6,000,000	$ 9,000,000
AJU Life Science Overseas Expansion Platform Fund(1)	4,000,000	6,000,000
Total	10,000,000	$ 15,000,000

(1) See “Principal Stockholders” for more information about shares held by this entity.
(2) Dr. Chan and Ms. O’Brien are members of our board of directors who have been designated by MVIL.

Series D Convertible Preferred Stock Financings

In closings that occurred in December 2015 and January 2016, we issued and sold an aggregate of 21,099,351 shares of our series D convertible preferred stock at a price per share of $2.234, for an aggregate purchase price of $47.1 million. The following table sets forth the number of shares of our series D convertible preferred stock purchased in these closings by directors, executive officers or 5% stockholders at the time of the transactions and their respective affiliates and the aggregate purchase price paid for such shares. Upon the closing of our initial public offering, all of the outstanding shares of our series D convertible preferred stock converted into shares of our common stock.

Name	Shares of Series D Convertible Preferred Stock Purchased	Aggregate Purchase Price
Morningside Venture Investments, Ltd.(1)(2)	4,476,275	$ 9,999,998
venBio Global Strategic Fund II LP(1)(3)	6,714,413	14,999,998
Cormorant Private Health Care Fund I, LP(1)(4)	3,357,206	7,499,998
Cormorant Global Healthcare Master Fund(1)(4)	1,119,069	2,500,000
Hillhouse WHP Holdings Ltd.(1)	4,476,275	9,999,998
AJU Life Science Overseas Expansion Platform Fund(1)	888,969	1,985,957
Epidarex Capital I, LP(1)(5)	67,144	150,000
Total	21,099,351	$ 47,135,950

(1) See “Principal Stockholders” for more information about shares held by this entity.
(2) Dr. Chan and Ms. O’Brien are members of our board of directors who have been designated by MVIL.

(3) Robert Adelman was a member of our board of directors who was designated by venBio.
(4) Bihua Chen was a member of our board of directors who was designated by Cormorant.
(5) Mr. Dunlop is a member of our board of directors who is an affiliate of Epidarex.

Series E Convertible Preferred Stock Financing

In August 2017, we issued and sold an aggregate of 7,792,035 shares of our series E convertible preferred stock at a price per share of $2.571, for an aggregate purchase price of $20.0 million. The following table sets forth the number of shares of our series E convertible preferred stock purchased by directors, executive officers or 5% stockholders at the time of the transactions and their respective affiliates and the aggregate purchase price paid for such shares. Upon the closing of our initial public offering, all of the outstanding shares of our series E convertible preferred stock converted into shares of our common stock.

Name	Shares of Series E Convertible Preferred Stock Purchased	Aggregate Purchase Price
Morningside Venture Investments, Ltd.(1)(2)	259,302	$ 666,665
venBio Global Strategic Fund II LP(1)(3)	648,256	1,666,666
venBio Select Fund LLC(1)(3)	388,953	999,998
Cormorant Private Health Care Fund I, LP(1)(4)	523,986	1,347,168
Cormorant Global Healthcare Master Fund(1)(4)	102,878	264,499
CRMA SPV LP(1)(4)	21,392	54,998
New Emerging Medical Opportunities Fund III, L.P. (Sectoral) (1)(5)	1,037,209	2,666,664
Sectoral Asset Management Holding Ltd.(1)(5)	259,302	666,665
Epidarex Capital I, LP(1)(6)	12,965	33,333
Total	3,254,242	$ 8,366,658

(1) See “Principal Stockholders” for more information about shares held by this entity.
(2) Dr. Chan and Ms. O’Brien are members of our board of directors who have been designated by MVIL.
(3) Dr. Adelman was a member of our board of directors who was designated by venBio.
(4) Ms. Chen was a member of our board of directors who was designated by Cormorant.
(5) Maha Katabi, Ph.D. was a member of our board of directors who was designated by Sectoral.
(6) Mr. Dunlop is a member of our board of directors who is an affiliate of Epidarex.

Participation in Initial Public Offering

In November 2017, we completed our initial public offering in which we issued and sold an aggregate of 10,714,000 shares of our common stock at a price to the public of $14.00 per share. In addition, in December 2017, we issued and sold an additional 981,107 shares of its common stock at a price to the public of $14.00 per share pursuant to the underwriters’ partial exercise of their over-allotment option. Certain of our 5% stockholders and their affiliates purchased an aggregate of 3,202,514 shares of our common stock in the initial public offering. Each of those purchases was made through the underwriters at the initial public offering price. The following table sets forth the number of shares of our common stock purchased by our directors and 5% stockholders and their affiliates and the aggregate purchase price paid for such shares.

Name	Shares of Common Stock Purchased	Aggregate Purchase Price
Hillhouse WHP Holdings Limited(1)	1,428,571	$ 19,999,994
Cormorant Funds(1)	1,071,428	14,999,992
Morningside Venture Investments, Ltd.(1)(2)	575,000	8,050,000
VenBio Global Strategic Fund(1)	127,515	1,785,210

(1) Ms. Chen was a member of our board of directors who was designated by Cormorant.
(2) See “Principal Stockholders” for more information about shares held by this entity.
(3) Dr. Chan and Ms. O’Brien are members of our board of directors who have been designated by MVIL.
(4) Dr. Adelman was a member of our board of directors who was designated by venBio.

Potentia Transactions

Dr. Francois and Messrs. Machiels and Dunlop, members of our board of directors, are members of the board of directors of Potentia. Dr. Francois, our Chief Executive Officer, is also the Chief Executive Officer of Potentia. Dr. Deschatelets, our Chief Operating Officer, is also the Chief Operating Officer of Potentia. These officers and directors beneficially own, in the aggregate, approximately 28.6% of the outstanding common stock of Potentia.

In September 2014, we entered into an asset purchase agreement with Potentia pursuant to which we agreed to acquire the assets of Potentia, primarily consisting of its license agreement with Penn, providing us with an exclusive license, under specified patent rights controlled by Penn, to develop and commercialize products covered by the licensed patent rights for ophthalmic indications. In September 2015, we completed the purchase of Potentia’s assets. Upon the closing, we issued to Potentia 3,844,352 shares of our common stock. If, as we expect, Potentia distributes the shares of our common stock it holds to its stockholders, a portion of those shares will be distributed to certain of our officers and directors at a future time. The allocation of these shares to Potentia stockholders upon distribution is substantially dependent upon the valuation of the shares at the time such shares are distributed to the stockholders of Potentia.

Danforth Advisors

In August 2015, we engaged Danforth Advisors, LLC, or Danforth, a consulting firm specializing in providing financial and strategic support to life sciences companies and a controlled affiliate of Daniel Geffken, who served as our interim Chief Financial Officer from August 2015 until October 2017. Pursuant to a consulting agreement effective September 2015, we paid professional fees to Danforth of $114,654 in 2015 and $173,304 in 2016 and $236,295 in 2017. Mr. Geffken was granted options with an aggregate grant date fair value of $87,750, as computed in accordance with ASC Topic 718.

Employment Relationship with Federico Grossi

Federico Grossi, our Executive Vice President of Clinical Development, is the brother-in-law of Dr. Francois. Dr. Grossi has been an employee since September 2014 and currently receives an annual salary of $300,000. Since September 1, 2014 and as of December 31, 2017, Dr. Grossi has received total salary compensation of $653,687, total bonus compensation of $214,228 and has been granted options with an aggregate grant date fair value of $631,501, as computed in accordance with ASC Topic 718.

Investors’ Rights Agreement

We are a party to an investors’ rights agreement, dated as of August 7, 2017, with certain holders of our common stock, including some of our directors and 5% stockholders and their affiliates and entities affiliated with our officers and directors. The investors’ rights agreement provides these holders the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing. See “Description of Capital Stock—Registration Rights” for additional information regarding these registration rights.

Indemnification Agreements

Our restated certificate of incorporation provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. In addition, we have entered into indemnification agreements with each

of our directors and executive officers. See “Executive Compensation—Limitations on Liability and Indemnification” for additional information regarding these agreements.

Policies and Procedures for Related Person Transactions

Our board of directors has adopted written policies and procedures, which became effective as of the date of our initial public offering, for the review of any transaction, arrangement or relationship in which our company is a participant, the amount involved exceeds $120,000 and one of our executive officers, directors, director nominees or 5% stockholders, or their immediate family members, each of whom we refer to as a “related person,” has a direct or indirect material interest.

If a related person proposes to enter into such a transaction, arrangement or relationship, which we refer to as a “related person transaction,” the related person must report the proposed related person transaction to our principal financial officer. The policy calls for the proposed related person transaction to be reviewed and approved by our audit committee. Whenever practicable, the reporting, review and approval will occur prior to entry into the transaction. If advance review and approval is not practicable, the committee will review, and, in its discretion, may ratify the related person transaction. The policy also permits the chairman of the audit committee to review and, if deemed appropriate, approve proposed related person transactions that arise between committee meetings, subject to ratification by the committee at its next meeting. Any related person transactions that are ongoing in nature will be reviewed annually.

A related person transaction reviewed under the policy will be considered approved or ratified if it is authorized by the audit committee after full disclosure of the related person’s interest in the transaction. As appropriate for the circumstances, the committee will review and consider:

- the related person’s interest in the related person transaction;
- the approximate dollar value of the amount involved in the related person transaction;
- the approximate dollar value of the amount of the related person’s interest in the transaction without regard to the amount of any profit or loss;
- whether the transaction was undertaken in the ordinary course of our business;
- whether the terms of the transaction are no less favorable to us than terms that could have been reached with an unrelated third party;
- the purpose of, and the potential benefits to us of, the transaction; and
- any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

The audit committee may approve or ratify the transaction only if the committee determines that, under all of the circumstances, the transaction is in our best interests. The committee may impose any conditions on the related person transaction that it deems appropriate.

The policy provides that transactions involving compensation of executive officers shall be reviewed and approved by the compensation committee in the manner specified in its charter.

PRINCIPAL STOCKHOLDERS

The following table sets forth information with respect to the beneficial ownership of our common stock as of February 28, 2018 by:

- each of our directors;
- each of our named executive officers;
- all of our directors and executive officers as a group; and
- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock.

The column entitled "Percentage of Shares Beneficially Owned—Before Offering" is based on a total of 50,372,762 shares of our common stock outstanding as of February 28, 2018. The column entitled "Percentage of Shares Beneficially Owned—After Offering" is based on 55,872,762 shares of our common stock to be outstanding after this offering, including the 5,500,000 shares of our common stock that we are selling in this offering, but not including any additional shares issuable upon exercise of outstanding options or warrants or any exercise by the underwriters of their option to purchase additional shares.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Shares of our common stock subject to options or warrants that are currently exercisable or exercisable within 60 days after February 28, 2018 are considered outstanding and beneficially owned by the person holding the options for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise set forth below, the address of the beneficial owner is c/o Apellis Pharmaceuticals, Inc., 6400 Westwind Way, Suite A, Crestwood, Kentucky 40014.

Name of Beneficial Owner	Shares Beneficially Owned	Percentage of Shares Beneficially Owned	
		Before Offering	After Offering
5% Stockholders			
Morningside Venture Investments, Ltd.(1)	11,353,303	22.5%	20.3%
Potentia Holdings, LLC(2)	3,826,601	7.6	6.8
venBio Global Strategic Fund II, LP(3)	3,579,305	7.1	6.4
Cormorant Funds(4)	3,768,756	7.5	6.7
Hillhouse Funds(5)	3,527,152	7.0	6.3
Named Executive Officers and Directors			
Cedric Francois, M.D., Ph.D.(6)(13)	1,740,482	3.4	3.1
Pascal Deschatelets, Ph.D.(7)(13)	1,317,588	2.6	2.3
Timothy Sullivan	—	—	—
Gerald Chan, D.Sc.(8)	86,342	*	*
Sinclair Dunlop(9)(13)	673,394	1.3	1.2
Alec Machiels(10)(13)	890,627	1.8	1.6
Stephanie Monaghan O'Brien(11)	86,342	*	*
All Executive Officers and Directors as a Group (11 persons)(12)	4,913,932	9.2	8.4

* Represents beneficial ownership of less than 1% of our outstanding stock.

(1) Louise Mary Garbarino, Jill Marie Franklin, Peter Stuart Allenby Edwards and Raymond Long Sing Tang, the directors of MVIL, share voting and dispositive control over the shares held by MVIL. The address for

MVIL is 2nd Floor, Le Prince de Galles, 3-5 Avenue des Citronniers, MC 98000, Monaco. We obtained the information regarding beneficial ownership of these shares solely from a Schedule 13G that was filed with the SEC on February 14, 2018.

(2) Potentia's board of directors has voting and dispositive control over the shares held by Potentia. The members of the Potentia board of directors are Cedric Francois, Alec Machiels, David Darst Jr., Stephen Gilles, Marie-Claude Bernal, Doug Onsi and Sinclair Dunlop. Because the board of directors acts by majority approval, none of the members of Potentia's board of directors has individual voting or investment power with respect to such shares. We expect that Potentia may distribute the shares of our common stock it holds to its stockholders at a future time. See "Transactions with Related Persons" for more information. We obtained the information regarding beneficial ownership of these shares solely from a Schedule 13G that was filed with the SEC on February 8, 2018.

(3) venBio Global Strategic GP II, L.P., or the General Partner, is the sole general partner of venBio Global Strategic Fund II LP, or venBio. venBio Global Strategic GP II, Ltd., or GP Ltd., is the sole general partner of the General Partner. Robert Adelman and Corey Goodman are directors of the GP Ltd. As the sole general partner of the Fund, the General Partner may be deemed to own beneficially the venBio Shares. As the sole general partner of the General Partner, the GP Ltd. likewise may be deemed to own beneficially the venBio Shares. As directors of the GP Ltd., each of the Directors likewise may be deemed to own beneficially the venBio Shares. The address for venBio, the General Partner and GP Ltd. is c/o venBio Partners, LLC, 1700 Owens Street, Suite 595, San Francisco, CA 94158. We obtained the information regarding beneficial ownership of these shares solely from a Schedule 13G that was filed with the SEC on February 9, 2018.

(4) Consists of shares of common stock beneficially owned by Cormorant Global Healthcare Master Fund, LP, or the Master Fund, and shares of common stock beneficially owned by Cormorant Private Healthcare Fund I, LP, or Fund I, and a managed account, or the Account. Cormorant Global Healthcare GP, LLC serves as the general partner of the Master Fund. Cormorant Asset Management, LLC serves as the investment manager to the Master Fund, Fund I and the Account. Bihua Chen serves as the managing member of Cormorant Global Healthcare GP, LLC and Cormorant Asset Management, LLC and may be deemed to have sole voting and investment power of the securities held by the Master Fund, Fund I and the Account. The address of the Master Fund, Fund I, the Account and Cormorant Asset Management, LLC is 200 Clarendon Street, 52nd Floor, Boston, MA 02116. We obtained the information regarding beneficial ownership of these shares solely from the Amendment No. 1 to Schedule 13G that was filed with the SEC on February 14, 2018.

(5) Consists of shares of common stock beneficially owned by Hillhouse WHP Holdings Limited, or WHP, Gaoling Fund, L.P., or Gaoling, and YHG Investment, L.P., or YHG. WHP is owned by Hillhouse Fund II, L.P., or Fund II. Hillhouse Capital Management, Ltd., or Hillhouse Capital, acts as the sole management company of Fund II and Gaoling and sole general partner of YHG. Hillhouse Capital is deemed to be the sole beneficial owner of, and to solely control the voting and investment power of, the shares of Common Stock held by Fund II, Gaoling and YHG. The address for Hillhouse Capital is Suite 1608, One Exchange Square, 8 Connaught Place, Hong Kong. We obtained the information regarding beneficial ownership of these shares solely from a Schedule 13G that was filed with the SEC on February 14, 2018.

(6) Consists of (i) 329,996 shares of common stock held by Dr. Francois, (ii) 234,411 shares of common stock held by The Francois-DuBois Educational Trust, as to which Mr. Machiels holds a voting proxy and for which Fiduciary Trust Company of New England serves as trustee, and (iii) 1,176,075 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2018.

(7) Consists of (i) 561,452 shares of common stock and (ii) 756,136 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2018.

(8) Consists of 86,342 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2018.

(9) Consists of (i) 186,371 shares of common stock held by MASA Life Science Ventures, LP, or MASA, (ii) 400,681 shares of common stock held by Epidarex Capital I, LP, or Epidarex, and (iii) 86,342 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2018. Mr. Dunlop is managing partner of MASA and general partner of Epidarex, and may be deemed to have voting and investment power over the shares held by each of MASA and Epidarex. The address for MASA is 7910 Woodmont Avenue, Suite 1210, Bethesda, MD 20814. The address for Epidarex is 7910 Woodmont Avenue, Suite 1210, Bethesda, MD 20814.

(10) Consists of (i) 382,345 shares of common stock, (ii) 234,411 shares of common stock held by The Francois-DuBois Educational Trust, as to which Mr. Machiels holds a voting proxy, and (iii) 273,871 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2018.

(11) Consists of 86,342 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2018.

(12) Consists of (i) 2,143,242 shares of common stock and (ii) 2,770,690 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2018.

(13) See “Transactions with Related Persons” for information regarding the possible distribution of a portion of the shares of our common stock held by Potentia to Drs. Francois and Deschatelets, and Messrs. Machiels and Dunlop, which shares are not reflected in these beneficial ownership amounts.

DESCRIPTION OF CAPITAL STOCK

General

Our authorized capital stock consists of 200,000,000 shares of common stock, par value $0.0001 per share, and 10,000,000 shares of preferred stock, par value $0.0001 per share, all of which preferred stock is undesignated. The following description of our capital stock and provisions of our restated certificate of incorporation and amended and restated bylaws are summaries and are qualified by reference to the certificate of incorporation and the bylaws. We have filed copies of these documents as exhibits to our registration statement of which this prospectus forms a part.

Common Stock

As of February 28, 2018, we had outstanding 50,372,762 shares of common stock, held by 112 stockholders of record.

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders will be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Other matters shall be decided by the affirmative vote of our stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter, except as otherwise disclosed below. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of outstanding preferred stock.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

Under the terms of our restated certificate of incorporation, our board of directors is authorized to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, antidilution provisions, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. As of the date of this prospectus, we have no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

Stock Options

As of February 28, 2018, options to purchase 7,396,674 shares of our common stock at a weighted-average exercise price of $6.33 per share were outstanding, of which options to purchase 3,373,956 shares of our common stock were exercisable, at a weighted-average exercise price of $3.75 per share, and options to purchase 2,078,522 shares of common stock were available for future issuance.

Warrants

In October 2017, we issued a warrant to purchase 14,064 shares of our common stock to Silicon Valley Bank in connection with entering into a term loan facility with Silicon Valley Bank. This warrant is exercisable at an exercise price of $5.484 per share.

The warrant has a ten-year term and includes a put option pursuant to which, in the event of an acquisition, change in control or dissolution or winding up of our company, or the expiration of the warrant, Silicon Valley Bank may require us to repurchase the warrant for a total aggregate purchase price of $250,000.

Registration Rights

Our investors' rights agreement provides specified holders of shares of our common stock, including some of our directors and 5% stockholders and their respective affiliates and entities affiliated with our officers and directors, the right to require us to register such shares under the Securities Act under specified circumstances as described below. After registration pursuant to these rights, these shares will become freely tradable without restriction under the Securities Act.

In connection with this offering, the necessary percentage of holders of registrable securities waived the rights to notice of this offering and to include their shares of registrable securities in this offering.

Demand Registration Rights

Beginning six months after the closing of our initial public offering, subject to specified limitations set forth in the investors' rights agreement, at any time the holders of a majority of then outstanding registrable securities, as defined in the investors' rights agreement, acting together, may demand in writing that we register their registrable securities under the Securities Act so long as the total amount of registrable shares requested to be registered has an anticipated aggregate offering price to the public, net of selling expenses, of least $5.0 million. We are not obligated to file a registration statement pursuant to this demand provision on more than two occasions, subject to specified exceptions.

In addition, at any time after we become eligible to file a registration statement on Form S-3 under the Securities Act, subject to specified limitations, the holders of at least 30% of the registrable securities then outstanding may demand in writing that we register on Form S-3 registrable shares held by them so long as the total amount of registrable shares requested to be registered has an anticipated aggregate offering price to the public, net of selling expenses, of least $1.0 million.

Incidental Registration Rights

If we propose to file a registration statement to register any of our securities under the Securities Act, either for our own account or for the account of any of our stockholders that are not holders of registrable shares, solely for cash and on a form that would also permit the registration of registrable shares, the holders of our registrable shares are entitled to notice of registration and, subject to specified exceptions, we will be required to register the registrable shares then held by them that they request that we register.

Expenses

Pursuant to the investors' rights agreement, we are required to pay all registration expenses, including registration fees, printing expenses, fees and disbursements of our counsel and accountants and reasonable fees and disbursements of one counsel representing the selling stockholders, other than any underwriting discounts and commissions, related to any demand or incidental registration. The investors' rights agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling

stockholders in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions in the registration statement attributable to them.

Anti-Takeover Effects of Delaware Law and Our Charter and Bylaws

Delaware law contains, and our restated certificate of incorporation and our amended and restated bylaws contain, provisions that could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors.

Staggered Board; Removal of Directors

Our restated certificate of incorporation and amended and restated bylaws divides our board of directors into three classes with staggered three-year terms. In addition, a director may only be removed for cause and only by the affirmative vote of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast in an annual election of directors. Any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may only be filled by vote of a majority of our directors then in office. The classification of our board of directors and the limitations on the removal of directors and filling of vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Stockholder Action by Written Consent; Special Meetings

Our restated certificate of incorporation provides that any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting of such holders and may not be effected by any consent in writing by such holders. Our restated certificate of incorporation and bylaws also provide that, except as otherwise required by law, special meetings of our stockholders can only be called by our chairman of the board, our Chief Executive Officer or our board of directors.

Advance Notice Requirements for Stockholder Proposals

Our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of persons for election to our board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors or by a stockholder of record on the record date for the meeting who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities.

Delaware Business Combination Statute

We are subject to Section 203 of the General Corporation Law of the State of Delaware. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our board of directors or unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Amendment of Certificate of Incorporation and Bylaws

The General Corporation Law of the State of Delaware provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our bylaws may be amended or repealed by a majority vote of our board of directors or by the affirmative vote of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast in any annual election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our restated certificate of incorporation described above under "—Staggered Board; Removal of Directors" and "—Stockholder Action by Written Consent; Special Meetings."

Exclusive Forum Selection

Our restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or if the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware) shall be the sole and exclusive forum for (1) any derivative action or proceeding brought on behalf of our company, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or employees to our company or our stockholders, (3) any action asserting a claim against our company arising pursuant to any provision of the General Corporation Law of the State of Delaware or our restated certificate of incorporation or bylaws, or (4) any action asserting a claim against our company governed by the internal affairs doctrine. Although our restated certificate of incorporation contains the choice of forum provision described above, it is possible that a court could rule that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

Listing on the Nasdaq Global Select Market

Our common stock is listed on the Nasdaq Global Select Market under the symbol "APLS."

Authorized but Unissued Shares

The authorized but unissued shares of common stock and preferred stock are available for future issuance without stockholder approval, subject to any limitations imposed by the listing requirements of the Nasdaq Global Select Market. These additional shares may be used for a variety of corporate finance transactions, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could make it more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

SHARES ELIGIBLE FOR FUTURE SALE

Future sales of substantial amounts of our common stock in the public market, including shares issued upon exercise of outstanding options or warrants, or the anticipation of these sales, could adversely affect market prices prevailing from time to time and could impair our ability to raise capital through sales of equity securities. Although our common stock is listed on the Nasdaq Global Select Market, we cannot assure you that there will continue to be an active public market for our common stock.

Upon the closing of this offering, we will have outstanding 55,872,762 shares of our common stock, based upon the 50,372,762 shares of our common stock that were outstanding on February 28, 2018, and after giving effect to the issuance of 5,500,000 shares of our common stock in this offering, and assuming no exercise by the underwriters of their option to purchase additional shares and no exercise of options or warrants outstanding as of February 28, 2018. All of shares, including the shares sold in this offering, will be freely tradable without restriction under the Securities Act except for any shares held by our "affiliates," as that term is defined in Rule 144 under the Securities Act. Approximately 13.7 million shares will be subject to the 90-day lock-up period under the lock-up agreements entered into in connection with this offering, and approximately 38.5 million are subject to the 180-day lock-up period under the lock-up agreements entered into in connection with our initial public offering, in each case as described below. Upon expiration of the applicable lock-up periods, these restricted securities may be sold in the public market only if registered or pursuant to an exemption from registration, such as Rule 144 or Rule 701 under the Securities Act.

Rule 144

In general, under Rule 144, any person who is not our affiliate and has held their shares for at least six months, including the holding period of any prior owner other than one of our affiliates, may sell shares without restriction, subject to the availability of current public information about us. In addition, under Rule 144, any person who is not our affiliate and has not been our affiliate at any time during the preceding three months and has held their shares for at least one year, including the holding period of any prior owner other than one of our affiliates, is entitled to sell an unlimited number of shares without regard to whether current public information about us is available.

A person who is our affiliate or who was our affiliate at any time during the preceding three months may sell any unrestricted securities, as well as restricted securities that the person has beneficially owned for at least six months, including the holding period of any prior owner other than one of our affiliates, under Rule 144. Affiliates selling restricted or unrestricted securities may sell a number of shares within any three-month period that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately 559,000 shares immediately after this offering; and
- the average weekly trading volume of our common stock on the Nasdaq Global Select Market during the four calendar weeks preceding the filing of a Notice of Proposed Sale of Securities Pursuant to Rule 144 with respect to the sale.

Sales under Rule 144 by our affiliates are also subject to manner of sale provisions and notice requirements and to the availability of current public information about us. We cannot estimate the number of shares of our common stock that our existing stockholders will elect to sell under Rule 144.

Rule 701

In general, under Rule 701 of the Securities Act, any of our employees, consultants or advisors, other than our affiliates, who purchased shares from us in connection with a qualified compensatory stock plan or other written agreement before our initial public offering is eligible to resell these shares in reliance on Rule 144, but

without compliance with the holding period requirements of Rule 144 and without regard to the volume of such sales or the availability of public information about us. Subject to the 180-day lock-up period under the lock-up agreements entered into in connection with our initial public offering as described below, approximately 47,613 shares of our common stock are eligible for sale in accordance with Rule 701.

Lock-Up Agreements

Lock-Up Agreements Entered into in Connection with this Offering

In connection with this offering, we and each of our executive officers and directors have agreed that, without the prior written consent of Citigroup Global Markets, Inc., J.P. Morgan Securities LLC and Cowen and Company, LLC on behalf of the underwriters, we and they will not, subject to limited exceptions, during the period ending 90 days after the date of this prospectus:

- offer, sell, contract to sell, pledge or otherwise dispose of, or enter into any transaction which is designed to, or might reasonably be expected to, result in the disposition of (whether by actual disposition or effective economic disposition due to cash settlement or otherwise), directly or indirectly, including the filing (or participation in the filing) of a registration statement (other than a registration statement on Form S-8) with the SEC with respect to, any shares of our capital stock or any securities convertible into, or exercisable or exchangeable for, such capital stock;
- establish or increase a put equivalent position or liquidate or decrease a call equivalent position with respect to any shares of our capital stock or any securities convertible into or exercisable or exchangeable for such capital stock, or publicly announce an intention to effect any such transaction; or
- publicly announce an intention to effect any of the foregoing.

Lock-Up Agreements Entered into in Connection with Our Initial Public Offering

Additionally, in connection with our initial public offering, we and each of our executive officers and directors and the holders of substantially all of our outstanding stock have agreed that, without the prior written consent of Citigroup Global Markets, Inc., J.P. Morgan Securities LLC and Cowen and Company, LLC on behalf of the underwriters, we and they will not, subject to limited exceptions, during the period ending May 6, 2018, which is 180 days after the date of the initial public offering prospectus:

- offer, sell, contract to sell, pledge or otherwise dispose of, or enter into any transaction which is designed to, or might reasonably be expected to, result in the disposition of (whether by actual disposition or effective economic disposition due to cash settlement or otherwise), directly or indirectly, including the filing (or participation in the filing) of a registration statement (other than a registration statement on Form S-8) with the SEC with respect to, any shares of our capital stock or any securities convertible into, or exercisable or exchangeable for, such capital stock;
- establish or increase a put equivalent position or liquidate or decrease a call equivalent position with respect to any shares of our capital stock or any securities convertible into or exercisable or exchangeable for such capital stock, or publicly announce an intention to effect any such transaction; or
- publicly announce an intention to effect any of the foregoing.

Registration Rights

Subject to the lock-up agreements described above, as of the date of this prospectus, the holders of an aggregate of 11,178,984 shares of our common stock are entitled to various rights with respect to the registration of these shares under the Securities Act. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. See “Description of Capital Stock—Registration Rights” for additional information. Shares covered by a registration statement will be eligible for sale in the public market upon the expiration or release from the terms of lock-up agreements applicable to such shares.

Stock Options and Warrants

As of February 28, 2018, we had outstanding options to purchase 7,396,674 shares of our common stock, of which options to purchase 3,373,956 shares were vested. We have filed a registration statement on Form S-8 under the Securities Act to register all of the shares of our common stock subject to outstanding options and options and other awards issuable pursuant to our 2017 plan, our 2017 ESPP and our 2010 plan. Accordingly, shares of our common stock registered under the registration statement on Form S-8 are eligible for sale in the public markets, subject to vesting restrictions, any applicable lock-up agreements described above and Rule 144 limitations applicable to affiliates.

In October 2017, we issued two warrants to purchase an aggregate of 107,828 shares of our common stock. A warrant as to 93,764 shares was exercised prior to our initial public offering. Any shares acquired through the exercise of these warrants will be eligible for sale subject to the lock-up agreements and securities laws described above.

MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF COMMON STOCK

The following is a general discussion of material U.S. federal income and estate tax considerations relating to ownership and disposition of our common stock by a non-U.S. holder. For purposes of this discussion, the term "non-U.S. holder" means a beneficial owner (other than a partnership or other pass-through entity) of our common stock that is not, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity treated as a corporation, created or organized in or under the laws of the United States or of any state thereof or the District of Columbia;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust if (1) a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or (2) the trust has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

This discussion does not address the tax treatment of partnerships or other entities that are pass-through (or disregarded) entities for U.S. federal income tax purposes or persons who hold their common stock through partnerships or such other pass-through or disregarded entities. The tax treatment of a partner in an entity or arrangement that is treated as a partnership for U.S. federal income tax purposes generally will depend upon the status of the partner and the activities of the partnership. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, and current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus, and all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change could alter the tax consequences to non-U.S. holders described in this prospectus. There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described in this prospectus.

We assume in this discussion that each non-U.S. holder holds shares of our common stock as a capital asset (generally, property held for investment) for U.S. federal income tax purposes. This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any aspects of U.S. state, local or non-U.S. taxes, the alternative minimum tax, or the Medicare tax on net investment income. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- financial institutions;
- brokers or dealers in securities;
- tax-exempt organizations;
- pension plans;
- owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment;
- traders in securities that have elected the mark-to-market method of accounting for their securities holdings;

- insurance companies;
- controlled foreign corporations;
- passive foreign investment companies;
- persons that have a functional currency other than the U.S. dollar;
- persons who have acquired our common stock pursuant to the exercise of an option or otherwise in a compensatory transaction;
- non-U.S. governments; and
- certain U.S. expatriates.

THIS DISCUSSION IS FOR GENERAL INFORMATION ONLY AND IS NOT, AND IS NOT INTENDED TO BE, LEGAL OR TAX ADVICE. PROSPECTIVE INVESTORS SHOULD CONSULT THEIR OWN TAX ADVISORS REGARDING THE U.S. FEDERAL, STATE, LOCAL, ESTATE AND NON-U.S. INCOME AND OTHER TAX CONSIDERATIONS OF ACQUIRING, HOLDING AND DISPOSING OF OUR COMMON STOCK.

Distributions on Our Common Stock

As discussed under "Dividend Policy" above, we do not expect to make cash dividends to holders of our common stock in the foreseeable future. Distributions, if any, on our common stock generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to the holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below under the heading "Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock." Any such distributions will also be subject to the discussion below under the headings "Information Reporting and Backup Withholding" and "FATCA."

Dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States, and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements (generally including provision of a valid IRS Form W-8ECI (or applicable successor form) certifying that the dividends are effectively connected with the non-U.S. holder's conduct of a trade or business within the United States). However, such U.S. effectively connected income, net of specified deductions and credits, is taxed in the hands of the non-U.S. holder at the same graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is classified as a corporation for U.S. federal income tax purposes may also be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their own tax advisors regarding their entitlement to benefits under a relevant income tax treaty and the specific methods available to them to satisfy these requirements.

A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS.

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

Subject to the discussion below under the headings "Information Reporting and Backup Withholding" and "FATCA," a non-U.S. holder generally will not be subject to U.S. federal income tax or withholding tax on any gain realized upon such non-U.S. holder's sale, exchange or other taxable disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed on a net income basis at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in "Distributions on Our Common Stock" also may apply;
- the non-U.S. holder is a non-resident alien individual present in the United States for a period or periods aggregating 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) on the net gain derived from the disposition, which may be offset by certain U.S.-source capital losses of the non-U.S. holder recognized in the taxable year of the disposition, if any; or
- we are, or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation" unless our common stock is regularly traded on an established securities market and the non-U.S. holder holds no more than 5% of our outstanding common stock, directly or indirectly, at any time during the shorter of the five-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a "U.S. real property holding corporation" if the fair market value of its "U.S. real property interests" (as defined in the Code and applicable regulations) equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we believe that we are not currently, and we do not anticipate becoming, a "U.S. real property holding corporation" for U.S. federal income tax purposes. If we are a U.S. real property holding corporation and either our common stock is not regularly traded on an established securities market or a non-U.S. holder holds more than 5% of our outstanding common stock, directly or indirectly, during the applicable testing period, such non-U.S. holder's gain on the disposition of shares of our common stock generally will be taxed in the same manner as gain that is effectively connected with the conduct of a U.S. trade or business, except that the branch profits tax generally will not apply. If we are a U.S. real property holding corporation and our common stock is not regularly traded on an established securities market, a non-U.S. holder's proceeds received on the disposition of shares will also generally be subject to withholding at a rate of 15%. Prospective investors are encouraged to consult their own tax advisors regarding the possible consequences to them if we are, or were to become, a U.S. real property holding corporation.

Information Reporting and Backup Withholding

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders generally will have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Generally, a non-U.S. holder will comply with such procedures if it

provides a properly executed IRS Form W-8BEN or W-8BEN-E (or other applicable Form W-8), or otherwise meets the documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption (and the payor does not have actual knowledge or reason to know that such holder is a United States person). Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above under "Distributions on Our Common Stock," will generally be exempt from U.S. backup withholding.

Information reporting and backup withholding, currently at a rate of 28%, generally will apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, whether U.S. or non-U.S., unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption from backup withholding. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

FATCA

The Foreign Account Tax Compliance Act, or FATCA, generally imposes a 30% withholding tax on dividends on, and gross proceeds from the sale or disposition of, our common stock paid to a foreign entity unless (i) if the foreign entity is a "foreign financial institution," the foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a "foreign financial institution," the foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt from FATCA.

Withholding under FATCA generally applies (1) to payments of dividends on our common stock, and (2) to payments of gross proceeds from a sale or other disposition of our common stock made after December 31, 2018. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this section. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of the tax. Non-U.S. holders should consult their own tax advisors regarding the possible implications of FATCA on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

U.S. Federal Estate Tax

Shares of our common stock that are beneficially owned or treated as beneficially owned at the time of death by an individual who is not a citizen or resident of the United States (as specially defined for U.S. federal estate tax purposes) are considered U.S. situs assets and will generally be included in the individual's gross estate for U.S. federal estate tax purposes. Such shares, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise. A non-U.S. holder is urged to consult his, her or its tax advisor regarding the U.S. federal estate tax consequences of the ownership or disposition of our common stock.

The preceding discussion of material U.S. federal tax considerations is for general information only. It is not legal or tax advice. Prospective investors should consult their own tax advisors regarding the particular U.S. federal, state, local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed or recently enacted changes in applicable laws.

UNDERWRITING

Citigroup Global Markets Inc., J.P. Morgan Securities LLC and Cowen and Company, LLC are acting as joint book-running managers of this offering and as representatives of the underwriters named below. Subject to the terms and conditions stated in the underwriting agreement dated the date of this prospectus, the underwriters named below have severally agreed to purchase, and we have agreed to sell to them, the number of shares of our common stock indicated below:

Underwriter	Number of Shares
Citigroup Global Markets Inc.	2,062,500
J.P. Morgan Securities LLC	2,062,500
Cowen and Company, LLC	1,375,000
Total	5,500,000

The underwriting agreement provides that the obligations of the underwriters to purchase the shares of our common stock included in this offering are subject to approval of legal matters by counsel and to other conditions. The underwriters are obligated to purchase all of the shares of our common stock (other than those covered by the underwriters' option to purchase additional shares described below) if they purchase any of the shares.

Shares of our common stock sold by the underwriters to the public will initially be offered at the public offering price set forth on the cover page of this prospectus. Any shares of our common stock sold by the underwriters to securities dealers may be sold at a discount from the public offering price not to exceed $0.918 per share. After the initial offering of the shares of our common stock, if all the shares of our common stock are not sold at the public offering price, the underwriters may change the offering price and the other selling terms. Sales of shares made outside of the United States may be made by affiliates of the underwriters.

If the underwriters sell more shares of our common stock than the total number set forth in the table above, we have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to 825,000 additional shares of our common stock at the public offering price less the underwriting discount. To the extent the option is exercised, each underwriter must purchase a number of additional shares of our common stock approximately proportionate to that underwriter's initial purchase commitment set forth in the table above. Any shares of our common stock issued or sold under the option will be issued and sold on the same terms and conditions as the other shares of our common stock that are the subject of this offering.

We, our officers and directors, and certain of our stockholders, have agreed that, subject to specified limited exceptions, for a period of 90 days from the date of this prospectus, we and they will not, without the prior written consent of Citigroup Global Markets Inc., J.P. Morgan Securities LLC and Cowen and Company, LLC, offer, sell, contract to sell, pledge or otherwise dispose of, or hedge any shares of our capital stock or any securities convertible into, or exercisable or exchangeable for, our capital stock. Citigroup Global Markets Inc., J.P. Morgan Securities LLC and Cowen and Company, LLC in their sole discretion may release any of the securities subject to these lock-up agreements at any time, which, in the case of officers and directors, shall be with notice. See "Shares Eligible for Future Sale" for more information.

Our common stock is listed on the Nasdaq Global Select Market, or Nasdaq, under the symbol "APLS."

The following table shows the per share and total underwriting discounts and commissions that we are to pay to the underwriters in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares:

	Per Share		Total	
	No Exercise	Full Exercise	No Exercise	Full Exercise
Public offering price	$ 25.50	$ 25.50	$140,250,000	$161,287,500
Underwriting discounts and commissions paid by us	$ 1.53	$ 1.53	$ 8,415,000	$ 9,677,250
Proceeds to us, before expenses	$ 23.97	$ 23.97	$131,835,000	$151,610,250

We estimate that expenses payable by us in connection with this offering, exclusive of underwriting discounts and commissions payable by us, will be approximately $500,000. We have also agreed to reimburse the underwriters for expenses in an amount up to $30,000 relating to the clearance of this offering with the Financial Industry Regulatory Authority, Inc.

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

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

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

In addition, certain of the underwriters may engage in passive market making transactions in our common stock on Nasdaq prior to the pricing and completion of this offering. Passive market making consists of displaying bids on Nasdaq no higher than the bid prices of independent market makers and making purchases at prices no higher than these independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are generally limited to a specified percentage of the passive market maker's average daily trading volume in the common stock during a specified period and must be discontinued when such limit is reached. Passive market making may cause the price of our common stock to be higher than the price that

otherwise would exist in the open market in the absence of these transactions. If passive market making is commenced, it may be discontinued at any time.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make because of any of those liabilities.

A prospectus in electronic format may be made available on websites maintained by one or more of the underwriters or their respective affiliates. The representatives may agree with us to allocate a number of shares of our common stock to underwriters for sale to their online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' or their respective affiliates' websites and any information contained in any other website maintained by any of the underwriters or their respective affiliates is not part of this prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors in this offering.

Conflicts of Interest

The underwriters are full-service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, principal investment, hedging, financing and brokerage activities. The underwriters and their respective affiliates may, from time to time, engage in transactions with and perform services for us in the ordinary course of their business for which they may receive customary fees and reimbursement of expenses. In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (which may include bank loans or credit default swaps) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

Notice to Prospective Investors in the European Economic Area

In relation to each member state of the European Economic Area that has implemented the Prospectus Directive (each, a relevant member state), with effect from and including the date on which the Prospectus Directive is implemented in that relevant member state (the relevant implementation date), an offer of shares of our common stock described in this prospectus may not be made to the public in that relevant member state other than:

- to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- to fewer than 100 or, if the relevant member state has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the relevant Dealer or Dealers nominated by us for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares of our common stock shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

For purposes of this provision, the expression an "offer of securities to the public" in any relevant member state means the communication in any form and by any means of sufficient information on the terms of the offer

and the shares of our common stock to be offered so as to enable an investor to decide to purchase or subscribe for any shares of our common stock, as the expression may be varied in that member state by any measure implementing the Prospectus Directive in that member state, the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the relevant member state) and includes any relevant implementing measure in the relevant member state, and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

The sellers of the shares of our common stock have not authorized and do not authorize the making of any offer of shares of our common stock through any financial intermediary on their behalf, other than offers made by the underwriters with a view to the final placement of the shares of our common stock as contemplated in this prospectus. Accordingly, no purchaser of the shares of our common stock, other than the underwriters, is authorized to make any further offer of the shares of our common stock on behalf of the sellers or the underwriters.

Notice to Prospective Investors in the United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, or the Order, or (ii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (each such person being referred to as a relevant person).

This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

Notice to Prospective Investors in Australia

No prospectus or other disclosure document (as defined in the Corporations Act 2001 (Cth) of Australia, or Corporations Act) in relation to our common stock has been or will be lodged with the Australian Securities & Investments Commission, or ASIC. This document has not been lodged with ASIC and is only directed to certain categories of exempt persons. Accordingly, if you receive this document in Australia:

- you confirm and warrant that you are either:
  - a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;
  - a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to us which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;
  - a person associated with the company under section 708(12) of the Corporations Act; or
  - a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act, and to the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act any offer made to you under this document is void and incapable of acceptance; and
- you warrant and agree that you will not offer any of our common stock for resale in Australia within 12 months of that common stock being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

Notice to Prospective Investors in France

Neither this prospectus nor any other offering material relating to the shares of our common stock described in this prospectus has been submitted to the clearance procedures of the *Autorité des Marchés Financiers* or of

the competent authority of another member state of the European Economic Area and notified to the *Autorité des Marchés Financiers*. The shares of our common stock have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France. Neither this prospectus nor any other offering material relating to the shares of our common stock has been or will be:

- released, issued, distributed or caused to be released, issued or distributed to the public in France; or
- used in connection with any offer for subscription or sale of the shares of our common stock to the public in France.

Such offers, sales and distributions will be made in France only:

- to qualified investors (*investisseurs qualifiés*) and/or to a restricted circle of investors (*cercle restreint d'investisseurs*), in each case investing for their own account, all as defined in, and in accordance with articles L.411-2, D.411-1, D.411-2, D.734-1, D.744-1, D.754-1 and D.764-1 of the French Code monétaire et financier;
- to investment services providers authorized to engage in portfolio management on behalf of third parties; or
- in a transaction that, in accordance with article L.411-2-II-1°-or-2°-or 3° of the French Code *monétaire et financier* and article 211-2 of the General Regulations (*Règlement Général*) of the *Autorité des Marchés Financiers*, does not constitute a public offer (*appel public à l'épargne*).

The shares of our common stock may be resold directly or indirectly, only in compliance with articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French Code *monétaire et financier*.

Notice to Prospective Investors in Chile

The shares of our common stock are not registered in the Securities Registry (Registro de Valores) or subject to the control of the Chilean Securities and Exchange Commission (Superintendencia de Valores y Seguros de Chile). This prospectus and other offering materials relating to the offer of the shares do not constitute a public offer of, or an invitation to subscribe for or purchase, the shares in the Republic of Chile, other than to individually identified purchasers pursuant to a private offering within the meaning of Article 4 of the Chilean Securities Market Act (Ley de Mercado de Valores) (an offer that is not "addressed to the public at large or to a certain sector or specific group of the public").

Notice to Prospective Investors in Hong Kong

The shares of our common stock may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), or (ii) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong) and no advertisement, invitation or document relating to the shares of our common stock may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares of our common stock which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Notice to Prospective Investors in the State of Israel

In the State of Israel this prospectus shall not be regarded as an offer to the public to purchase shares of common stock under the Israeli Securities Law, 5728 - 1968, which requires a prospectus to be published and

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

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

Notice to Prospective Investors in Japan

The shares of our common stock offered in this prospectus have not been and will not be registered under the Financial Instruments and Exchange Law of Japan. The shares of our common stock have not been offered or sold and will not be offered or sold, directly or indirectly, in Japan or to or for the account of any resident of Japan (including any corporation or other entity organized under the laws of Japan), except (i) pursuant to an exemption from the registration requirements of the Financial Instruments and Exchange Law and (ii) in compliance with any other applicable requirements of Japanese law.

Notice to Prospective Investors in Singapore

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

Where the shares of our common stock are subscribed or purchased under Section 275 of the SFA by a relevant party which is:

- a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, shares, debentures and units of shares of our common stock and debentures of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares of our common stock pursuant to an offer made under Section 275 of the SFA except:
  - to an institutional investor (for corporations, under Section 274 of the SFA) or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares of our common stock and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than $200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions specified in Section 275 of the SFA;
  - where no consideration is or will be given for the transfer; or
  - where the transfer is by operation of law.

Notice to Prospective Investors in Canada

The securities may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the securities must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the representatives are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

LEGAL MATTERS

The validity of the shares of our common stock offered hereby is being passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP. Cooley LLP is acting as counsel for the underwriters in connection with this offering.

EXPERTS

The consolidated financial statements of Apellis Pharmaceuticals, Inc. at December 31, 2016 and 2017, and for each of the three years in the period ended December 31, 2017, appearing in this prospectus and registration statement have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon (which contains an explanatory paragraph describing conditions that raise substantial doubt about the Company's ability to continue as a going concern as described in Note 1 to the consolidated financial statements) appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of our common stock we are offering to sell. This prospectus, which constitutes part of the registration statement, does not include all of the information contained in the registration statement and the exhibits, schedules and amendments to the registration statement. For further information with respect to us and our common stock, we refer you to the registration statement and to the exhibits and schedules to the registration statement. Statements contained in this prospectus about the contents of any contract, agreement or other document are not necessarily complete, and, in each instance, we refer you to the copy of the contract, agreement or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference to such contract, agreement or document.

We are subject to the reporting and information requirements of the Exchange Act and, as a result, file, or will file, periodic reports, proxy statements and other information with the SEC. These periodic reports and other information are available for inspection and copying at the SEC's public reference room and the website of the SEC, in each case, referred to above. We also maintain a website at http://www.apellis.com and make available free of charge through this website our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act. We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. The information contained on, or that can be accessed through, our website is not a part of this prospectus. The reference to our web address does not constitute incorporation by reference of the information contained in, or that can be accessed through, our website.

You may read and copy this information at the SEC's public reference room, which is located at 100 F Street, N.E., Room 1580, Washington, DC 20549. You can request copies of the registration statement by writing to the Securities and Exchange Commission and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the SEC's public reference room. In addition, the SEC maintains an Internet website, which is located at *www.sec.gov*, that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC. You may access the registration statement of which this prospectus is a part at the SEC's Internet website.

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of
Apellis Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Apellis Pharmaceuticals, Inc. (the Company) as of December 31, 2017 and 2016, the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity and cash flows for each of the three years in the period ended December 31, 2017, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has recurring losses from operations and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2015.

Louisville, Kentucky

March 19, 2018

APELLIS PHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS

	December 31, 2016	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	$ 24,863,488	$ 175,643,529
Refundable research and development credit	1,347,804	1,297,361
Prepaid assets	1,132,438	5,059,593
Other current assets	25,000	14,823
Total current assets	27,368,730	182,015,306
Other assets	64,528	116,150
Total assets	$ 27,433,258	$ 182,131,456
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 2,547,212	$ 3,663,253
Accrued expenses	1,091,726	2,890,705
Total current liabilities	3,638,938	6,553,958
Long-term liabilities:		
Term loan facility	—	19,806,944
Promissory note - related party	—	6,583,402
Common stock warrant liability	—	244,292
Total liabilities	3,638,938	33,188,596
Stockholders' equity:		
Series A convertible preferred stock, $0.0001 par value; 2,670,000 shares authorized, issued and outstanding at December 31, 2016 and zero shares authorized, issued and outstanding at December 31, 2017	2,654,405	—
Series B convertible preferred stock, $0.0001 par value; 6,362,658 shares authorized, issued and outstanding at December 31, 2016 and zero shares authorized, issued and outstanding at December 31, 2017	6,944,148	—
Series C convertible preferred stock, $0.0001 par value; 26,215,411 shares authorized, issued and outstanding at December 31, 2016 and zero shares authorized, issued and outstanding at December 31, 2017	35,542,707	—
Series D convertible preferred stock, $0.0001 par value; 21,099,351 shares authorized, issued and outstanding at December 31, 2016 and zero shares authorized, issued and outstanding at December 31, 2017	46,913,666	—
Preferred stock, $0.0001 par value; zero shares authorized, issued and outstanding at December 31, 2016 and 10,000,000 shares authorized, and zero shares issued and outstanding at December 31, 2017	—	—
Common stock, $0.0001 par value; 87,000,000 shares authorized and 8,428,366 shares issued and outstanding at December 31, 2016 and 200,000,000 shares authorized and 50,334,152 shares issued and outstanding at December 31, 2017	843	5,033
Additional paid in capital	29,996,110	298,201,480
Accumulated deficit	(98,257,559)	(149,263,653)
Total stockholders' equity	23,794,320	148,942,860
Total liabilities and stockholders' equity	$ 27,433,258	$ 182,131,456

See accompanying notes to consolidated financial statements

APELLIS PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

	Year Ended December 31,		
	2015	2016	2017
Operating expenses:			
Research and development	$ 13,730,311	$ 22,978,599	$ 40,303,878
Cost of acquired in-process research and development	26,486,000	—	—
General and administrative	6,356,782	4,303,743	10,463,151
Operating loss	(46,573,093)	(27,282,342)	(50,767,029)
Loss from remeasurement of fair value of warrants	—	—	(153,692)
Interest income (expense), net	50,853	135,309	(96,915)
Other income, net	6,284	22,396	11,542
Net loss and comprehensive loss	$ (46,515,956)	$ (27,124,637)	$ (51,006,094)
Net loss per common share, basic and diluted	$ (8.03)	$ (3.22)	$ (3.68)
Weighted-average number of common shares used in net loss per common share, basic and diluted	5,795,040	8,428,366	13,870,949

See accompanying notes to consolidated financial statements

APELLIS PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY

	Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Equity
	Outstanding Shares	Amount	Outstanding Shares	Amount			
Balance at January 1, 2015	29,064,736	$ 35,866,260	4,583,282	$ 458	$ 1,974,955	$ (24,616,966)	$ 13,224,707
Issuance of common stock upon exercise of stock options	—	—	732	1	1,718	—	1,719
Issuance of Series C convertible preferred stock, net of issuance costs	6,183,333	9,277,112	—	—	—	—	9,277,112
Series C tranche Right	—	(2,112)	—	—	—	—	(2,112)
Issuance of common stock upon closing Potentia asset purchase, net of issuance costs	—	—	3,844,352	384	26,394,748	—	26,395,132
Issuance of Series D convertible preferred stock, net of issuance costs	14,384,938	32,050,646	—	—	—	—	32,050,646
Share-based compensation expense	—	—	—	—	545,701	—	545,701
Net loss	—	—	—	—	—	(46,515,956)	(46,515,956)
Balance at December 31, 2015	49,633,007	77,191,906	8,428,366	843	28,917,122	(71,132,922)	34,976,949
Issuance of Series D convertible preferred stock, net of issuance costs	6,714,413	14,863,020	—	—	—	—	14,863,020
Share-based compensation expense	—	—	—	—	1,078,988	—	1,078,988
Net loss	—	—	—	—	—	(27,124,637)	(27,124,637)
Balance at December 31, 2016	56,347,420	92,054,926	8,428,366	843	29,996,110	(98,257,559)	23,794,320
Issuance of Series E convertible preferred stock, net of issuance costs	7,792,035	19,747,847	—	—	—	—	19,747,847
Issuance of common stock upon exercise of stock options	—	—	46,881	5	164,496	—	164,501
Issuance of warrants to an affiliate of stockholder	—	—	—	—	430,160	—	430,160
Issuance of common stock upon exercise of warrants	—	—	93,764	9	514,191	—	514,200
Conversion of convertible preferred stock to common stock	(64,139,455)	(111,802,773)	30,070,034	3,007	111,799,766	—	—
Issuance of common stock in initial public offering, net of issuance costs	—	—	11,695,107	1,169	149,878,047	—	149,879,216
Share-based compensation expense	—	—	—	—	5,418,710	—	5,418,710
Net loss	—	—	—	—	—	(51,006,094)	(51,006,094)
Balance at December 31, 2017	—	$ —	50,334,152	$ 5,033	298,201,480	$(149,263,653)	$148,942,860

See accompanying notes to consolidated financial statements

APELLIS PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year Ended December 31,		
	2015	2016	2017
Operating Activities			
Net loss	$ (46,515,956)	$ (27,124,637)	$ (51,006,094)
Adjustments to reconcile net loss to net cash used in operating activities:			
Non-cash acquisition of in-process research and development	26,486,000	—	—
Share-based compensation expense	545,701	1,078,988	5,418,710
Loss from remeasurement of fair value of warrants	—	—	153,692
Accretion of discounts	—	—	13,563
Amortization	—	—	11,935
Changes in operating assets and liabilities:			
Refundable research and development credit	(1,313,398)	408,934	50,443
Prepaid assets	(190,926)	(873,884)	(3,927,155)
Other current assets	110,054	—	10,177
Other assets	(96,050)	68,743	(51,622)
Accounts payable	1,725,904	69,779	932,299
Accrued expenses	392,724	368,999	1,798,979
Net cash used in operating activities	(18,855,947)	(26,003,078)	(46,595,073)
Financing Activities			
Issuance of Series C convertible preferred stock, net of issuance costs	9,275,001	—	—
Issuance of Series D convertible preferred stock, net of issuance costs	32,050,646	14,863,020	—
Issuance of Series E convertible preferred stock, net of issuance costs	—	—	19,747,847
Deferred issuance costs	(90,868)	—	—
Proceeds from issuance of term loan, net of issuance costs	—	—	19,795,007
Proceeds from issuance of promissory note payable to an affiliate of stockholder	—	—	6,569,840
Proceeds from issuance of common stock, net of issuance costs	1,719	—	150,062,959
Proceeds from the issuance of common stock warrants	—	—	520,760
Proceeds from exercise of stock options and warrants	—	—	678,701
Net cash provided by financing activities	41,236,498	14,863,020	197,375,114
Net increase (decrease) in cash and cash equivalents	22,380,551	(11,140,058)	150,780,041
Cash and cash equivalents at beginning of period	13,622,995	36,003,546	24,863,488
Cash and cash equivalents at end of period	$ 36,003,546	$ 24,863,488	$ 175,643,529
Supplemental Disclosure of Non-Cash Financing Activities			
Conversion of convertible preferred stock to common stock	$ —	$ —	$ 111,802,773

See accompanying notes to consolidated financial statements

APELLIS PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of Organization and Operations

Apellis Pharmaceuticals, Inc. (the "Company") is a clinical-stage biopharmaceutical company focused on the development of novel therapeutic compounds to treat disease through the inhibition of the complement system, which is an integral component of the immune system, at the level of C3, the central protein in the complement cascade.

The Company was incorporated in September 2009 under the laws of the State of Delaware. The Company's principal executive offices are located in Crestwood, Kentucky.

The Company's operations since inception have been limited to organizing and staffing the Company, acquiring rights to product candidates, business planning, raising capital and developing its product candidates.

The Company is subject to risks common in the biotechnology industry including, but not limited to, raising additional capital, development by its competitors of new technological innovations, its ability to successfully complete preclinical and clinical development of product candidates and receive timely regulatory approval of products, market acceptance of the Company's products, protection of proprietary technology, healthcare cost containment initiatives, and compliance with governmental regulations, including those of the U.S. Food and Drug Administration ("FDA").

Initial Public Offering

On November 13, 2017, the Company issued and sold 10,714,000 shares of its common stock at a price per share to the public of $14.00 in its initial public offering ("IPO"). The Company received net proceeds of $137.2 million after deducting underwriting discounts and commissions of $10.5 million and offering costs of $2.3 million. In addition, on December 13, 2017, the Company issued and sold an additional 981,107 shares of its common stock at the initial public offering price of $14.00 per share pursuant to the underwriters' partial exercise of their option to purchase additional shares of common stock, which resulted in net proceeds of approximately $12.8 million, after deducting underwriting discounts and commissions of $1.0 million.

Liquidity and Going Concern

The accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities and commitments in the normal course of business.

The Company is subject to risks common to other life science companies in the development stage including, but not limited to, uncertainty of product development and commercialization, lack of marketing and sales history, development by its competitors of new technological innovations, dependence on key personnel, market acceptance of products, product liability, protection of proprietary technology, ability to raise additional financing, and compliance with FDA and other government regulations. If the Company does not successfully commercialize any of its product candidates, it will be unable to generate recurring product revenue or achieve profitability. Management's plans in order to meet its short-term and longer term operating cash flow requirements include obtaining additional funding.

The uncertainties associated with the Company's ability to (1) obtain additional debt or equity financing on terms that are favorable to the Company, (2) enter into collaborative agreements with strategic partners, and (3) succeed in its future operations, raise substantial doubt about the Company's ability to continue as a going concern. The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or amounts of liabilities that might be necessary should the Company be

unable to continue its operations. If the Company is not able to obtain the required funding in the near future, or is not able to obtain funding on terms that are favorable to the Company, it will have a material adverse effect on its operations and strategic development plan for future growth. If the Company cannot successfully raise additional funding and implement its strategic development plan, then its liquidity, financial condition and business prospects will be materially and adversely affected, and the Company may have to cease operations.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements include the accounts of the Company and its wholly-owned subsidiary, Apellis Australia Pty Ltd. All intercompany balances and transactions have been eliminated in consolidation. The consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP") and following the requirements of the Securities and Exchange Commission (the "SEC").

Reclassifications

Certain prior year amounts have been reclassified to conform to the 2017 presentation.

Stock Split

On October 27, 2017, the Company effectuated a l-for-2.133 reverse stock split of its outstanding common stock, which was approved by the Company's board of directors on October 27, 2017. The reverse stock split resulted in an adjustment to the conversion prices of the Company's then outstanding series of convertible preferred stock to reflect a proportional decrease in the number of shares of common stock to be issued upon conversion. The accompanying financial statements and notes to the financial statements give retroactive effect to the reverse stock split for all periods presented. The shares of common stock retained a par value of $0.0001 per share. Accordingly, the stockholders' deficit reflects the reverse stock split by reclassifying from "common stock" to "additional paid-in capital" an amount equal to the par value of the decreased shares resulting from the reverse stock split.

Offering Costs

Offering costs represent underwriting, legal, accounting and other direct costs related to the Company's IPO. These costs were deferred until completion of the IPO, at which time they were reclassified to additional paid-in capital as a reduction of the proceeds.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses

APELLIS PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

during the reporting period. Actual results may differ from those estimates. Management considers many factors in selecting appropriate financial accounting policies and controls, and in developing the estimates and assumptions that are used in the preparation of these financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, including expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates, and whether historical trends are expected to be representative of future trends. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes, and management must select an amount that falls within that range of reasonable estimates. Estimates are used in the following areas, among others: share-based compensation expense, fair value of common stock and preferred stock, accrued expenses, prepaid expenses and income taxes.

Historically for all periods prior to the IPO, the Company utilized various valuation methodologies in accordance with the framework of the American Institute of Certified Public Accountants Technical Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, to estimate the retrospective fair value of its common stock during all periods presented. The methodologies include a probability analysis including both a potential public trading scenario and potential sale scenario. In both scenarios, value is estimated using the guideline public company method. The sale scenario includes an adjustment for a market participant acquisition premium. Value is allocated among the preferred and common shares according to the rights associated with each type of security. Valuation methodologies include estimates and assumptions that require the Company's judgment. These estimates include assumptions regarding future performance. Significant changes to the key assumptions used in the valuations could result in different fair values of common stock and the associated fair value of stock options granted at each valuation date. Since the completion of the IPO, the Company's board of directors determines the fair value of underlying common stock based upon the closing price of the Company's common stock as reported on the date of grant.

Fair Value of Financial Instruments

Management believes that the carrying amounts of the Company's financial instruments, including accounts payable and accrued expenses, approximate the fair value due to the short term nature of those instruments. The Company follows the fair value hierarchy within Accounting Standards Codification ("ASC") 820, Fair Value Measurements, and classifies its financial instruments as Level I.

Cash and Cash Equivalents

Cash and cash equivalents are defined as cash in banks and investment instruments having maturities of three months or less from their acquisition date. The carrying amounts reported in the consolidated balance sheets for cash and cash equivalents are valued at cost, which approximates their fair value.

Foreign Currency

The functional currency of the Company's wholly-owned subsidiary is the U.S. dollar.

Research and Development

Costs incurred in connection with research and development activities are expensed as incurred. Research and development expenses include (i) employee-related expenses, including salaries, benefits, travel and share-based compensation expense; (ii) external research and development expenses incurred under arrangements with third parties, such as contract research and contract manufacturing organizations, investigational sites and consultants, including share-based compensation expense for consultants; (iii) the cost of acquiring, developing and manufacturing clinical study materials; and (iv) costs associated with preclinical and clinical activities and regulatory operations.

APELLIS PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

The Company enters into consulting, research and other agreements with commercial entities, researchers, universities and others for the provision of goods and services. Such arrangements are generally cancellable upon reasonable notice and payment of costs incurred. Costs are considered incurred based on an evaluation of the progress to completion of specific tasks under each contract using information and data provided by the Company's clinical sites and vendors. These costs consist of direct and indirect costs associated with specific projects, as well as fees paid to various entities that perform certain research on behalf of the Company.

Depending upon the timing of payments to the service providers, the Company recognizes prepaid expenses or accrued expenses related to these costs. These accrued or prepaid expenses are based on management's estimates of the work performed under service agreements, milestones achieved and experience with similar contracts. The Company monitors each of these factors and adjusts estimates accordingly.

Included in research and development is a refundable Australian research and development credit. The credit is recognized as a reduction of clinical trial costs over the periods necessary to match the benefit of the credit with the costs for which it is intended to compensate.

During 2017, the Company identified and corrected an immaterial presentation error in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2015 and 2016. The error was the result of presenting $1.7 and $1.2 million of Australian research and development refundable credits for the years ended December 31, 2015 and 2016, respectively as an income tax benefit in the period. As the enacted legislation in Australia provides for the credit to be received without regard to taxable income the credit was incorrectly classified as an income tax benefit. Accordingly, we have reclassified the credits as a reduction of research and development operating expenses. Net loss and comprehensive loss was not impacted by this error and no other line items within any of the other consolidated financial statements and footnotes were impacted by this error, other than the Company's tax footnote.

Patents

Costs incurred in connection with the application for and issuance of patents are expensed as incurred.

Income Taxes

Income taxes are recorded in accordance with Financial Accounting Standards Board ("FASB") ASC Topic 740, *Income Taxes* ("ASC 740"), which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Valuation allowances are provided if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position, as well as consideration of the available facts and circumstances. As of December 31, 2016 and 2017, the Company did not have any significant uncertain tax positions.

Share-based Compensation

The Company accounts for its share-based compensation awards in accordance with FASB ASC Topic 718, *Compensation—Stock Compensation* ("ASC 718"). ASC 718 requires all share-based payments to employees,

APELLIS PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

including grants of employee stock options, be recognized in the statements of operations and comprehensive loss based on their estimated fair values over the requisite service periods for each award. The Company accounts for share-based awards to non-employees in accordance with FASB ASC Topic 505-50, *Equity-Based Payments to Non-Employees* ("ASC 505-50"), which requires the fair value of the award to be re-measured at fair value until a performance commitment is reached or counterparty performance is complete. The Company's share-based compensation awards are comprised of stock options. The Company estimates the fair value of each stock option grant using the Monte Carlo simulation model ("Monte Carlo") for grants made prior to June 30, 2015 and the Black-Scholes option pricing model ("Black-Scholes") for grants made on or after July 1, 2015 through October 2017. After the Company's IPO in November 2017, the Company's board of directors determined the fair value of underlying common stock based upon the closing price of the Company's common stock as reported on the date of the grant.

Both Monte Carlo and Black-Scholes for option pricing require the input of the six minimum considerations detailed in ASC 718, including (a) the expected stock price volatility, (b) the calculation of expected term of the award, (c) the risk-free interest rate and (d) expected dividends. Due to the lack of a public market for the trading of the Company's common stock and a lack of company-specific historical and implied volatility data, the Company has based its estimate of expected volatility on the historical volatility of a group of comparable companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The computation of expected volatility is based on the historical volatility of a representative group of companies with similar characteristics to the Company, including stage of product development and life science industry focus. The Company is in a very early stage of product development with no revenues, and the representative group of companies has similar characteristics. The Company believes the group selected has sufficient similar economic and industry characteristics. The Company calculated the expected term for options granted to employees based on a quarterly weighted average probability of exit analysis considering milestones that the Company had achieved and each of the potential exit scenarios available to the Company at that time. The expected term is applied to the stock option grant group as a whole, as the Company does not expect substantially different exercise or post-vesting termination behavior among its employee population. For options granted to non-employees, the Company utilizes the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected life of the stock options. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock.

The Company's share-based awards are subject to service based vesting conditions. Compensation expense related to awards to employees with service based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is generally the vesting term. Consistent with the guidance in ASC 505-50, compensation expense related to awards to non-employees with service based vesting conditions is recognized on a straight-line basis based on the then-current fair value at each financial reporting date prior to the measurement date over the associated service period of the award, which is generally the vesting term.

The Company recognizes forfeitures for employee and non-employee grants at the time they occur. Share-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest.

Concentrations of Credit Risk

Cash and accounts receivable are the only financial instruments that potentially subject the Company to concentrations of credit risk. The Company's cash is maintained with accredited financial institutions and is insured by the Federal Deposit Insurance Corporation.

APELLIS PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Net Loss per Share

Basic net loss per common share is calculated by dividing net loss by the weighted-average shares outstanding during the period. For purposes of the diluted net loss per share calculation, convertible preferred stock and common stock options are considered to be common stock equivalents but have been excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive for all periods presented. Therefore, basic and diluted net loss per share were the same for all periods presented.

Comprehensive Loss

The Company has no components of comprehensive loss other than its net loss and, accordingly, comprehensive loss is the same as the net loss for all periods presented.

Recent Accounting Pronouncements

In May 2014, the FASB issued Accounting Standards Update ("ASU") 2014-09, *Revenue from Contracts with Customers (Topic 606)*. The standard will apply one comprehensive revenue recognition model across all contracts, entities and sectors. The core principle of the new standard is that revenue should be recognized to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. ASU 2014-09 will replace most of the existing revenue recognition requirements in U.S. GAAP. The FASB also issued ASU 2015-14, *Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date*, which deferred the effective date of the standard for one year. As a result, the new standard is effective for annual reporting periods beginning after December 15, 2017, for public companies, including interim periods within that reporting period. As the Company does not currently have revenue, the adoption of the new standard will have no impact on its consolidated financial statements.

In August 2014, the FASB issued ASU 2014-15, *Presentation of Financial Statements—Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, which requires management to evaluate whether there are conditions and events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the financial statements are issued and, if so, to disclose that fact. Management is also required to evaluate and disclose whether its plans alleviate that doubt. The standard is effective for annual periods ending after December 15, 2016. With the adoption of the ASU 2014-15, the Company has expanded its disclosures within the *Liquidity and Going Concern* section of Note 1.

In November 2015, the FASB issued ASU 2015-17, *Income Taxes: Balance Sheet Classification of Deferred Taxes*. This ASU simplifies the presentation of deferred income taxes and requires that deferred tax liabilities and assets be classified as noncurrent amounts in the consolidated balance sheets. Such amounts were previously required to be classified as current and noncurrent assets and liabilities. The Company adopted ASU 2015-17 effective January 1, 2017; however, there was no impact to the financial statements as a result of this adoption as the Company has recorded full valuation allowances against all deferred tax assets.

In February 2016, the FASB issued ASU 2016-02, *Leases*, which establishes a comprehensive new lease accounting model. The new standard: (a) clarifies the definition of a lease; (b) requires a dual approach to lease classification similar to current lease classifications; and, (c) causes lessees to recognize leases on the balance sheet as a lease liability with a corresponding right-of-use asset for leases with a lease-term of more than twelve months. The new standard is effective for fiscal years and interim periods beginning after December 15, 2018 and requires modified retrospective application. Early adoption is permitted. The Company is currently evaluating the impact that the adoption of ASU 2016-02 will have on its consolidated financial statements.

APELLIS PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

In March 2016, the FASB issued ASU 2016-09, *Compensation—Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting*. The guidance simplified the accounting and financial reporting for share-based compensation arrangements. This guidance requires excess tax benefits to be recorded as a discrete item within income tax expense rather than additional paid-in-capital. In addition, excess tax benefits are required to be classified as cash from operating activities rather than cash from financing activities. The Company adopted the provisions of ASU 2016-09 effective January 1, 2017. The Company elected to apply the cash flow guidance of ASU 2016-09 retrospectively to all prior periods with no impact to historical periods. The Company also adopted a change in accounting policy to recognize forfeitures of awards as they occur instead of estimating potential forfeitures.

3. Asset Purchase From Related Party

In September 2014, the Company agreed to purchase substantially all of the assets of Potentia Pharmaceuticals, Inc. ("Potentia"), in exchange for 3,844,352 shares of common stock. In September 2015, the Company completed the acquisition and issued the shares, which the Company determined, with the assistance of a third-party specialist, to have a fair value of $26,486,000. As there were no integrated sets of activities and assets representing inputs and processes that would constitute a business under ASC 805, *Business Combinations* ("ASC 805"), the Company accounted for the transaction as an asset acquisition. In-process research and development expense of $26,486,000 was recognized in the Company's consolidated statement of operations and comprehensive loss in 2015.

Certain officers and members of the Board of Directors of the Company are directors and significant stockholders of Potentia. Under the asset purchase agreement, the Company agreed to make certain vendor payments on Potentia's behalf pending the closing of the transaction. The Company recognized expenses related to this arrangement of $874,427 for the year ended December 31, 2015.

4. Common Stock

The Company has reserved the following shares of common stock for future issuance:

	December 31,		
	2015	2016	2017
Conversion of Series A convertible preferred stock	1,251,758	1,251,758	—
Conversion of Series B convertible preferred stock	2,982,962	2,982,962	—
Conversion of Series C convertible preferred stock	12,290,394	12,290,394	—
Conversion of Series D convertible preferred stock	6,743,993	9,891,866	—
Shares reserved under 2010 Equity Incentive Plan	3,375,527	4,781,264	5,817,844
Shares reserved under 2017 Equity Incentive Plan	—	—	1,682,596
Shares reserved under 2017 Employee Stock Purchase Plan			468,823
Common stock warrants	—	—	14,064
Total	26,644,634	31,198,244	7,983,327

5. Convertible Preferred Stock

Authorized capital stock includes 56,347,420 shares of convertible preferred stock and 10,000,000 shares of preferred stock at December 31, 2016 and 2017, respectively.

Series C Convertible Preferred Stock

In January 2015, the Company issued 183,333 shares of Series C convertible preferred stock ("Series C Preferred") at $1.50 per share for aggregate proceeds of $275,000.

APELLIS PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Between March and May 2015, the Company issued 6,000,000 shares of Series C Preferred at $1.50 per share for aggregate proceeds of $9,000,000.

Series D Convertible Preferred Stock

In December 2015, the Company issued 14,384,938 shares of Series D convertible preferred stock ("Series D Preferred") at $2.234 per share for aggregate proceeds of $32,135,951, less issuance costs of $85,306.

In January 2016, the Company issued 6,714,413 shares of Series D convertible preferred stock at $2.234 per share for aggregate proceeds of $15,000,000, less issuance costs of $136,980.

Series E Convertible Preferred Stock

In August 2017, the Company issued 7,792,035 shares of Series E convertible preferred stock at $2.571 per share for aggregate proceeds of $20,033,322, less issuance costs of $285,475.

Upon closing of the Company's IPO on November 13, 2017, all shares of convertible preferred stock converted into shares of common stock.

6. Accrued Expenses

Accrued expenses are as follows:

	December 31,	
	2016	2017
Accrued research and development	$ 871,066	$ 2,463,808
Accrued payroll liabilities	91,598	251,491
Other	129,062	175,406
Total	$ 1,091,726	$ 2,890,705

7. Long-term Debt

Term Loan Facility

On October 20, 2017, the Company entered into a loan and security agreement with Silicon Valley Bank ("SVB") to provide for a $20.0 million term loan facility (the "term loan facility"). Borrowings under the term loan facility bear interest at a floating rate per annum equal to the WSJ prime rate plus 1.50%; provided, however, that in an event of default, as defined in the loan and security agreement, the interest rate applicable to borrowings under such agreement will be increased by 5.0%. Under the agreement, the Company is required to make monthly interest-only payments through November 1, 2019 and is required to make 24 equal monthly payments of principal, plus accrued interest, thereafter from November 1, 2019 through October 1, 2021, at which time all unpaid principal and interest becomes due and payable.

The Company may voluntarily prepay all, but not less than all, of the outstanding principal at any time prior to the maturity date, subject to a prepayment fee, which ranges from 0% to 2% of the outstanding principal. A final payment of $1.6 million is due upon the earlier to occur of the maturity of the loan, the acceleration or prepayment of all outstanding principal or the termination of the term loan facility.

Borrowings under the term loan facility are secured by a first priority lien on all of the Company's assets, excluding intellectual property owned by the Company. The Company has agreed to a negative pledge on its

intellectual property and to grant a security interest on its interest in its licenses from University of Pennsylvania ("Penn") (described in Note 8) if Penn consents to such security interest. The term loan facility contains customary events of default and affirmative and negative covenants, including restrictions on the Company's ability to pay dividends and incur additional debt, but does not contain any financial covenants.

In connection with the Company's entry into the term loan facility, the Company issued to SVB a warrant to purchase 14,064 shares of the Company's common stock with an exercise price per share of $5.484. The warrant has a ten-year term and includes a put option pursuant to which, in the event of an acquisition, change in control or dissolution or winding up of the Company or the expiration of the warrant, SVB may require the Company to repurchase the warrant for a total aggregate purchase price of $250,000. As the warrant may be put to the Company at SVB's option based on the passage of time (upon the expiration of the warrant), the Company has accounted for the warrant as a liability pursuant to ASC 480.

Related Party Promissory Note

On October 19, 2017, the Company issued and sold an unsecured promissory note in the principal amount of $7.0 million to Golda Darty Partners S.A. ("GDP"), an affiliate of one of the Company's stockholders. The promissory note bears interest at a rate per annum of 8.0%, and is due and payable quarterly in arrears on the 19th day of each April, July, October and January beginning on January 19, 2018. The promissory note has a maturity date of October 19, 2022. The promissory note is contractually subordinated to the term loan facility with SVB.

In connection with the issuance and sale of the above promissory note, the Company issued to GDP a warrant to purchase 93,764 shares of the Company's common stock at a price per share of $5.484, which was exercised in whole in October 2017. The Company recorded the fair value of the warrant in the aggregate amount of $430,160 as a discount to the promissory note. This amount is being accreted as additional interest expense over the term of the promissory note.

The contractual maturities of our long-term debt obligations due subsequent to December 31, 2017 are as follows:

2018	$ —
2019	1,666,667
2020	10,000,000
2021	8,333,333
2022	7,000,000
	$ 27,000,000

8. License Agreements

In connection with its purchase of assets from Potentia in September 2014, the Company became party to a license agreement with the Trustees of the University of Pennsylvania ("Penn") as a result of an agreement to purchase substantially all the assets of Potentia Pharmaceuticals, Inc, for an exclusive, worldwide license to specified patent rights. The Company is required to pay annual maintenance fees of $100,000 until the first sale of a licensed product. The Company is also required to make milestone payments aggregating up to $3,200,000 based upon the achievement of specified development and regulatory milestones and up to $5,000,000 based upon the achievement of specified annual sales milestones with respect to each licensed product, and to pay low single-digit royalties based on net sales of each licensed product and with minimum quarterly royalty thresholds. In addition, the Company is obligated to pay a specified portion of income it receives from sublicensees.

APELLIS PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

In addition, the Company is also party to a 2010 license agreement with Penn for an exclusive, worldwide license to specified patent rights for the development and commercialization of products in fields of use, as defined therein. The Company is required to pay annual maintenance fees of $100,000 until the first sale of a licensed product. The Company is required to make milestone payments aggregating up to $1,650,000, based upon the achievement of development and regulatory approval milestones, and up to $2,500,000, based upon the achievement of annual sales milestones with respect to each of the first two licensed products. There have been no events to date that would trigger milestone obligations under the agreement. The license agreement also requires the Company to pay low single digit royalties based on net sales of each licensed product, subject to minimum quarterly royalty thresholds. In addition, the Company is obligated to pay a specified portion of income it receives from sublicensees.

9. 401(k) Profit Sharing Plan and Trust

In July 2010, the Company adopted an employee profit-sharing plan (the “401(k) Plan”), qualified under Section 401(k) of the Internal Revenue Code (the “IRC”). All of the Company’s full-time employees who have attained the age of 21 are eligible to participate in the 401(k) Plan immediately upon employment. Pursuant to the 401(k) Plan, employees may elect to reduce their current compensation by up to the statutorily prescribed annual limit and have the amount of the reduction contributed to the 401(k) Plan. In 2016 and 2017, the Company recorded $50,867 and $123,264, respectively, for employer contributions made to the 401(k) Plan.

10. Refundable Research Development and Income Taxes

The Company earns non-income related refundable Australian research and development credits that are settled and paid to the Company annually. The associated income from the credits are an offset to research and development expenses.

The Company’s income tax provision is computed based on the federal statutory rate and the average state statutory rates, net of the related federal benefit. For the years ended December 31, 2016 and 2017, there was no current or deferred income tax expense or benefit due to the Company’s net losses and increases in its deferred tax asset valuation allowance.

APELLIS PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

The Company's effective income tax provision differs from the amount calculated using the statutory U.S. federal income tax rate, principally due to the following:

	Year Ended December					
	2017		2016		2015	
	Amount	Percentage of income before income taxes	Amount	Percentage of income before income taxes	Amount	Percentage of income before income taxes
Statutory U.S. federal income tax	$(17,852,133)	35.0%	$ (9,222,377)	34.0%	$(15,815,425)	34.0%
State income taxes, net of federal benefit	(1,634,924)	3.3	(992,768)	3.5	(685,158)	1.5
Change in valuation allowances	11,176,291	(20.8)	12,923,538	(46.4)	6,932,927	(14.9)
Re-measurement of deferred taxes	15,659,916	(31.9)	—	—	—	—
Tax credits	(3,316,729)	7.7	(2,933,836)	10.8	(488,588)	1.1
Acquisition Accounting	—	—	—	—	9,005,240	(19.4)
Permanent and other	(4,032,421)	6.7	225,443	(1.9)	1,051,004	(2.3)
Effective income tax provision	$ —	—%	$ —	—%	$ —	—%

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's deferred tax assets and liabilities are as follows:

	December 31,	
	2016	2017
Deferred tax assets:		
Accrual to cash adjustment	$ 914,627	$ 345,623
Intangible assets	41,166	23,543
Share-based compensation	1,000,887	1,826,372
Contribution carryforwards	23,371	24,465
Net operating loss carryforwards	22,704,142	30,699,411
Research and development credits	1,842,200	3,357,291
Orphan drug credits	3,502,686	4,928,666
Total deferred tax assets	30,029,079	41,205,371
Less valuation allowance	(30,029,079)	(41,205,371)
Net deferred tax assets	$ —	$ —

At December 31, 2016 and December 31, 2017, the Company had approximately $60,214,000 and $118,843,000, respectively, of net operating loss carryforwards. The Company also had $8,285,957 of federal research and development tax credit carryforwards as of December 31, 2017. The net operating loss and research and development tax credit carryforwards begin to expire in 2024.

The net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become

subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the IRC, respectively, as well as similar state provisions.

Under Section 382 of the Internal Revenue Code, as amended ("Section 382"), the Company's net operating loss carryforwards ("NOLs") and other deferred tax assets can generally be used to offset future taxable income and therefore reduce federal income tax obligations. However, the Company's ability to use its NOLs would be limited if there was an "ownership change" as defined by Section 382. This would occur if shareholders owning (or deemed to own under the tax rules) 5% or more of the Company's common stock increase their aggregate ownership of the common stock of the Company by more than 50 percentage points over a defined period of time. The Company had an ownership change on September 8, 2015. As a result, a portion of the NOL and tax credit carryforwards are subject to an annual utilization limitation.

The deferred tax asset includes approximately $30.7 million of NOLs and $8.3 million of research & development tax credit carryforwards. Of the $30.7 million of NOLs, approximately $12.3 million is limited under Section 382. Of the $8.3 million tax credit carryforwards, approximately $1.9 million is limited under Section 383. Subsequent ownership changes may further affect the limitation in future years.

Our estimate of the realizability of the deferred tax asset is dependent on our estimate of projected future levels of taxable income. In analyzing future taxable income levels, we considered all evidence currently available, both positive and negative. Based on our analysis, we have recorded a valuation allowance for all deferred tax assets as of December 31, 2016 and 2017.

Tax Act Enactment

On December 22, 2017, the U.S. government enacted comprehensive federal tax legislation commonly referred to as the Tax Cuts and Jobs Act of 2017 (the "Tax Act"). The Tax Act significantly modifies the U.S. corporate income tax system by, among other things, reducing the federal income tax rate from 35% to 21% beginning in 2018, imposing a mandatory one-time deemed repatriation tax on accumulated foreign earnings and creating a territorial tax system that changes the manner in which future foreign earnings are subject to U.S. tax. The Tax Act also provides that undistributed and previously untaxed post-1986 foreign earnings will be deemed distributed in 2017 and be subject to tax at reduced effective rates (the "Transition Tax"). The Company has a net cumulative deficit in earnings and profits from its foreign subsidiaries and, consequently, will not be subject to the Transition Tax. The company re-measured certain net deferred tax assets and liabilities based on the tax rates at which they are expected to reverse in the future. The total impact to the gross deferred tax asset balance (before valuation allowance) upon enactment of the Tax Act is $16 million, As there is a valuation allowance recorded for all deferred tax assets as of December 31, 2017, there was no impact to the net deferred tax assets balance. The estimated impacts of the Tax Act recorded during the year ended December 31, 2017 are provisional in nature, and the Company will continue to assess the impact of the U.S. Tax Reform Act and will record adjustments through the income tax provision in the relevant period as authoritative guidance is made available to the public.

The Company has generated research credits and orphan drug credits but has not conducted a detailed study to document its qualified activities. A detailed study could result in an adjustment to the Company's research and development credit carryforwards; however, until such a study is completed and any adjustment is identified, no amounts are being presented as an uncertain tax position.

The Company does not have any unrecognized tax benefits during any periods presented and does not expect this to significantly change in the next twelve months.

APELLIS PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

There were no interest and penalties recorded in the statement of operations during any period and no amounts accrued for interest and penalties at December 31, 2017, or 2016.

The Company files income tax returns in the U.S. federal jurisdiction, and applicable state jurisdictions. The Company's 2014 through 2017 tax years remain open and subject to examination by federal and state taxing authorities. Federal and state net operating losses are subject to review by taxing authorities in the year utilized.

11. Commitments and Contingencies

The Company leases office space in Crestwood, Kentucky under the terms of an operating lease, as amended. The lease expires in July 2018. In October 2016, the Company leased office space in Cambridge, Massachusetts under the terms of an operating lease. The lease expires in October 2018. In April 2017, the Company entered into a lease for office space in Waltham, Massachusetts (the "Waltham Lease"). The Waltham Lease has a term of 60 months and includes leasing 6,126 square feet of office space. The Waltham Lease provides for initial monthly lease payments of $17,612 per month. The base rent payable over the lease period is $1,117,995. In May 2017, the Company entered into a lease for office space in San Francisco, California (the "SF Lease"). The SF Lease has a term of 24 months and includes leasing 1,872 square feet of office space. The SF Lease provides for initial monthly lease payments of $7,800 per month. The base rent payable over the lease period is $182,208. Lease expense for the years ended December 31, 2015, 2016, and 2017 was $81,521, $117,222 and $351,468, respectively.

At December 31, 2017, the Company's future minimum payments required under these leases are as follows:

2018	$ 390,344
2019	260,196
2020	226,152
2021	232,278
2022	137,580
	$ 1,246,550

The Company contracts to conduct research and development activities with remaining contract costs of approximately $1,713,000 at December 31, 2017 that will be incurred in future periods. The scope of the services under the research and development contracts can be modified and the contracts cancelled by the Company upon written notice. In some instances, the contracts may be cancelled by the third party upon written notice.

Indemnifications—In the ordinary course of business, the Company enters into agreements that may include indemnification provisions. Pursuant to such agreements, the Company may indemnify, hold harmless and defend indemnified parties for losses suffered or incurred by the indemnified party. Some of the provisions will limit losses to those arising from third-party actions. In some cases, the indemnification will continue after the termination of the agreement. The maximum potential amount of future payments the Company could be required to make under these provisions is not determinable. The Company has never incurred any cost to defend lawsuits or settle claims related to these indemnification provisions.

Legal—During the normal course of business, the Company may be a party to legal claims that may not be covered by insurance. Management does not believe that any such claims would have a material impact on the Company's consolidated financial statements.

APELLIS PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

12. Equity Incentive Plans

Share-based Compensation

The Company's Board of Directors adopted, and its stockholders approved, an equity incentive plan in 2010 (as amended, the "2010 Plan"). The Board of Directors and stockholders amended the 2010 Plan in August 2017 to increase the number of shares of common stock reserved for issuance thereunder to 6,188,466. The 2010 Plan allowed for the grant of incentive stock options and non-qualified stock options to purchase common stock for employees, directors and consultants under terms and conditions established by the Board of Directors. Incentive stock options and nonqualified stock options were granted at exercise prices that were no less than 100% of the estimated fair value per share of the common stock on the date of grant. If an individual owns capital stock representing more than 10% of the voting shares, the price of each share was at least 110% of the fair value on the date of grant. The Board of Directors determined the fair value of common stock with the assistance of a third-party specialist. Options expire 10 years from the issuance date. Following the adoption of the 2017 Stock Incentive Plan, the Company no longer grants stock options or other awards under the 2010 Plan.

In October 2017, the Company's Board of Directors adopted, and its stockholders approved, the 2017 Stock Incentive Plan (the "2017 Plan"), which became effective on November 8, 2017. The 2017 Plan provides for the grant of incentive stock options, non-statutory stock options, stock appreciation rights, awards of restricted stock, restricted stock units and other stock-based awards. The number of shares of common stock reserved for issuance under the 2017 plan is the sum of (i) 1,359,587 shares of common stock, plus (ii) an additional number of shares of common stock equal to the sum of (a) the number of shares of common stock reserved for issuance under the 2010 equity incentive plan that remained available for future issuance immediately prior to the effectiveness of the 2017 Plan, which was 299,568 shares, and (b) the number of shares of common stock subject to outstanding awards under the 2010 equity incentive plan upon effectiveness of the 2017 plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by us at their original issuance price pursuant to a contractual repurchase right plus (iii) an annual increase, to be added the first day of each fiscal year, beginning with the fiscal year ending December 31, 2018 and continuing until, and including, the fiscal year ending December 31, 2027, equal to the lowest of 4,219,409 shares of common stock, 4.0% of the number of shares of common stock outstanding on the first day of the fiscal year and an amount determined by the board of directors.

Stock Options—Options granted generally vest over 48 months. Options granted to employees on or after December 5, 2013 generally vest in installments of (i) 25% at the one year anniversary and (ii) in either 36 equal monthly or 12 equal quarterly installments beginning in the thirteenth month after the initial vesting commencement date (as defined) subject to the employee's continuous service with the Company. Options granted before December 5, 2013 vest over four years in equal annual installments of 25% at each anniversary of the grant date.

The Company's options granted prior to February 2016 become fully vested upon the occurrence of a change in control, as defined in the 2010 Plan. Options granted to executives after February 2016 become vested and exercisable with respect to 50% of the then unvested options if such executive is terminated without cause or resigns for good reason within 12 months following a change of control. Options granted to Dr. Francois, Dr. Deschatelets and Mr. Sullivan will become fully vested upon the occurrence of a change in control. The balance of the Company's options do not receive additional vesting upon a change of control.

Effective January 22, 2016, the Board of Directors approved a modification in the exercise price of stock options to purchase 93,762 shares of common stock that were granted under the 2010 Plan to reduce the exercise price per share to $3.76 per share, which was the estimated fair market value of the common stock on the effective date of the repricing. Other stock options granted under the 2010 Plan were excluded from this repricing and will maintain their original exercise prices. The stock options that were repriced had been granted with an

exercise price greater than the estimated fair market value in July and September 2015 (i.e., exercise prices ranging from $6.81 to $6.89 per share). Because the exercise prices of these stock options exceeded the estimated fair market value of the Company's common stock on the modification date, the Board of Directors determined that the retentive value of these awards had substantially diminished from the time they had been granted. The Board of Directors determined that this repricing was in the best interests of the Company and its stockholders to provide a continued incentive for highly qualified employees and consultants with substantial experience in the Company's business to remain employed during a critical period for the Company.

The following table summarizes the Company's stock option activity:

	Shares	Weighted-Average Exercise Price Per Share	Weighted-Average Grant Date Fair Value Per Share	Weighted-Average Contractual Life (in years)	Aggregate Intrinsic Value
Outstanding, January 1, 2015	2,343,090	$ 2.50	$ 1.56	7.52	$ 578,128
Granted	210,970	4.82	3.26	9.50	65,000
Exercised	(732)	2.35	1.43	—	1,031
Forfeited	(79,113)	2.13	1.54	—	128,250
Outstanding, December 31, 2015	2,474,215	2.71	1.71	7.01	2,870,775
Granted	1,380,463	3.26	1.98	9.37	—
Forfeited	(23,441)	2.43	1.13	9.83	—
Outstanding, December 31, 2016	3,831,237	2.84	1.75	7.20	243,000
Granted	2,940,444	6.94	3.61	9.67	41,878,351
Exercised	(46,881)	3.51	2.25	—	852,818
Forfeited	(369,219)	2.56	1.22	—	7,066,915
Outstanding, December 31, 2017	6,355,581	4.78	2.66	7.64	107,534,863
Options exercisable, December 31, 2015	1,519,866	2.43	1.58	6.10	2,058,419
Expected to vest, December 31, 2015	954,349	3.16	1.90	8.46	812,365
Options exercisable, December 31, 2016	2,048,318	2.56	1.64	5.76	243,000
Expected to vest, December 31, 2016	1,782,919	3.16	1.90	8.85	—
Options exercisable, December 31, 2017	3,156,433	3.67	2.12	5.90	56,918,296
Expected to vest, December 31, 2017	3,199,149	5.88	3.19	9.35	50,616,567

The aggregate intrinsic values of options outstanding, exercisable, vested and expected to vest were calculated as the difference between the exercise price of the options and the estimated fair value of the common stock as of December 31, 2017. Estimated fair values of the common stock at the time of the grants between May 12, 2010 and December 31, 2017 were between $1.71 and $14.00.

Total share-based compensation expense recognized was as follows:

	Year Ended December 31,		
	2015	2016	2017
Research and development	$ 171,388	$ 377,776	$ 2,678,956
General and administrative	374,313	701,212	2,739,754
Total share-based compensation expense	$ 545,701	$ 1,078,988	$ 5,418,710

APELLIS PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

At December 31, 2015, 2016 and 2017, unrecognized compensation expense related to unvested options, net of estimated forfeitures, was $1,673,110, $2,910,870 and $10,415,787, respectively, which the Company expects to recognize over an estimated weighted-average period of 2.36, 2.85, and 3.14 years, respectively. As of December 31, 2017, the future amortization of unearned share-based compensation costs will be $4,693,212 in 2018, $2,548,514 in 2019, $1,949,248 in 2020 and $1,224,813 in 2021.

The assumptions used in the Monte Carlo and Black-Scholes models to estimate the grant date fair value are as follows:

	Year Ended December 31,		
	2015	2016	2017
Risk-free interest rate	1.61 - 1.87%	1.21 - 1.60%	1.21 - 2.30%
Dividend yield	0%	0%	0%
Volatility	78.1 - 93.5%	52.0 - 78.1%	51.6 - 55.8%
Expected terms (years)	5.4 - 6.2	5.2 - 5.7	5.3 - 7.0

2017 Employee Stock Purchase Plan

In October 2017, the Company's board of directors adopted and the Company's stockholders approved the 2017 Employee Stock Purchase Plan ("ESPP"), which became effective upon the IPO and provides participating employees with the opportunity to purchase up to an aggregate of 468,823 shares of our common stock. The number of shares of our common stock reserved for issuance under the 2017 ESPP will automatically increase on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2018 and continuing until, and including, the fiscal year ending December 31, 2027, equal to the lowest of (i) 937,646 shares of our common stock, (ii) 1.0% of the number of shares of our common stock outstanding on the first day of the fiscal year and (iii) an amount determined by our board of directors. The board of directors has not initiated any offerings under the ESPP.

13. Net Loss per Common Share

The following table presents the calculation of basic and diluted net loss per common share:

	Year Ended December 31,		
	2015	2016	2017
Numerator:			
Net loss and comprehensive loss	$ (46,515,956)	$ (27,124,637)	$ (51,006,094)
Denominator:			
Weighted-average number of common shares used in net loss per common share — basic and diluted	5,795,040	8,428,366	13,870,949
Net loss per common share — basic and diluted	$ (8.03)	$ (3.22)	$ (3.68)

Shares outstanding presented below were excluded from the calculation of diluted net loss per share, prior to the use of the treasury stock method, as their effect is anti-dilutive:

	Year Ended December 31,		
	2015	2016	2017
Convertible preferred stock	23,269,107	26,416,896	—
Common stock under option	2,474,215	3,831,237	6,355,581
Common stock warrants	—	—	14,064
Total	25,743,322	30,248,133	6,369,645

APELLIS PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

14. Selected Quarterly Financial Data (Unaudited)

The following interim financial information presents the Company's 2016 and 2017 results of operations on a quarterly basis:

	Quarter Ended			
	March 31, 2016	June 30, 2016	September 30, 2016	December 31, 2016
Net Operating Loss	$ (6,228,452)	$ (7,572,638)	$ (7,234,204)	$ (6,247,048)
Net Loss	(5,999,699)	(7,294,245)	(7,210,591)	(6,620,102)
Net Loss per common share, basic and diluted	(0.33)	(0.41)	(0.86)	(3.22)

	Quarter Ended			
	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
Net Operating Loss	$ (9,214,375)	$ (12,394,490)	$ (11,589,319)	$ (17,568,845)
Net Loss	(9,050,773)	(12,126,152)	(11,573,273)	(18,255,896)
Net Loss per common share, basic and diluted	(0.50)	(0.67)	(1.37)	(3.68)

15. Subsequent Events

In February 2018, the Company granted an aggregate of 1,126,585 options to purchase shares of common stock to employees with an exercise price ranging from $14.64 to $16.45.

5,500,000 Shares

Common Stock

$25.50 per share

PROSPECTUS

April 18, 2018

Citigroup

J.P. Morgan

Cowen