UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2019

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM _____ TO _____**

Commission File Number 001-38276

APELLIS PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its Charter)

DELAWARE	**27-1537290**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
100 Fifth Avenue Waltham, MA	**02451**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 977-5700

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.0001 par value per share	**APLS**	**Nasdaq Global Select Market**

Securities registered pursuant to Section 12(g) of the Act:
None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ☒ NO ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES ☐ NO ☒

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES ☒ NO ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). YES ☒ NO ☐

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

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Small reporting company	☐
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

As of June 30, 2019, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the closing price of the shares of common stock on the Nasdaq Global Select Stock Market on such date, was $1,151,210,910. The number of shares of the registrant's common stock, par value $0.0001 per share outstanding as of February 21, 2020 was 75,321,471.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A in connection with its 2020 Annual Meeting of Stockholders. Portions of such proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Annual Report contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report, 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 dosing of patients, enrollment and completion of these trials and of the anticipated results from these trials;
- our plans to initiate clinical trials of our current and future product candidates;
- the potential clinical benefits and attributes of our current and future product candidates and the inhibition of C3;
- our plans to develop our current and future product candidates 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 our current and future 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 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 Annual Report on Form 10-K, 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 Annual Report on Form 10-K and the documents that we have filed or incorporated by reference as exhibits to this Annual Report on Form 10-K 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 applicable law.

This Annual Report on Form 10-K 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 Annual Report on Form 10-K 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. The Apellis logo is our trademark. The other trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners.

PART I

Item 1. 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 programs targeting C3 with Phase 3 clinical trials of our lead product candidate, pegcetacoplan, formerly known as APL-2, in multiple indications. We believe that pegcetacoplan 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. Pegcetacoplan has already shown activity that we believe is clinically meaningful in clinical trials for several distinct medical conditions, including geographic atrophy in age-related macular degeneration, or GA; paroxysmal nocturnal hemoglobinuria, or PNH; cold agglutinin disease, or CAD; and C3 glomerulopathy, or C3G. We are developing compounds targeting C3, including APL-9, for intravenous administration and plan to conduct clinical trials of these compounds in additional complement-dependent indications. We hold worldwide commercialization rights to pegcetacoplan, APL-9 and other novel compounds targeting C3.

Intravitreal administration of pegcetacoplan.

We are developing pegcetacoplan for intravitreal administration in ophthalmological indications. We initiated a Phase 3 clinical program consisting of two Phase 3 clinical trials evaluating pegcetacoplan in patients with GA in September 2018, which we refer to as the DERBY and OAKS trials. We expect that both trials will be fully enrolled by the end of the first half of 2020 and that we will announce data from these trials in mid-2021. In our Phase 2 clinical trial of pegcetacoplan in patients with GA, treatment with pegcetacoplan resulted in a significant reduction in the rate of GA lesion growth over 12 months.

Subcutaneous administration of pegcetacoplan.

We are developing pegcetacoplan for subcutaneous administration in several indications, including PNH, CAD and C3G.

PNH. In June 2018, we initiated a Phase 3 clinical trial evaluating pegcetacoplan in patients with PNH who exhibited moderate to severe anemia (specifically with an inclusion criterion of hemoglobin level of less than 10.5 g/dL) while being treated with eculizumab, an approved therapy for PNH that is marketed as Soliris. We refer to this trial as the PEGASUS trial.

In January 2020, we announced top-line data from the PEGASUS trial that showed that pegcetacoplan met the trial's primary efficacy endpoint, demonstrating superiority to eculizumab with a statistically significant improvement in adjusted means of 3.8 g/dL of hemoglobin at week 16 ($p<0.0001$) and showing promising results in key secondary endpoints, including transfusion avoidance and absolute reticulocyte count. In the trial, the safety profile of pegcetacoplan was comparable to eculizumab. We plan to present detailed 16-week results from the PEGASUS trial at a future scientific meeting and expect to report 48-week topline data in the second half of 2020.

In September 2019 we initiated a second Phase 3 clinical trial in patients with PNH who have not been treated with eculizumab, or eculizumab treatment-naïve patients. We expect to complete enrollment in this trial in the first half of 2020 and to present top-line data in the first quarter of 2021. We refer to this trial as the PRINCE trial.

We intend to meet with regulatory agencies in the first half of 2020 to discuss what information is required to support regulatory submissions of a new drug application, or NDA, and a marketing authorization application, or MAA, for pegcetacoplan in PNH.

CAD. In our ongoing Phase 2 clinical trials of pegcetacoplan in patients with CAD, patients have achieved increased hemoglobin levels, reduced reticulocytes and bilirubin levels, and reduced LDH levels. We intend to disclose our plans and timing for further clinical development of pegcetacoplan for patients with CAD in the first half of 2020.

C3G. We are conducting a Phase 2 clinical trial of pegcetacoplan for C3G and other glomerular diseases with complement involvement. We presented preliminary data on patients with C3G from this trial at the Annual Meeting of American Society of Nephropathy in November 2019. We intend to disclose our plans and timing for further clinical development of pegcetacoplan for patients with C3G in the first half of 2020.

Intravenous C3 inhibition.

We are developing compounds targeting C3 for intravenous administration. In particular, we are developing APL-9 for the prevention of complement immune system activation coincident with adeno-associated virus, or AAV, vector administration for gene therapies and other indications. APL-9 is a second generation C3 modulator and is designed to be intravenously administered for acute use.

Our Programs

Our lead product candidate, pegcetacoplan, is a C3 inhibitor. Pegcetacoplan is a conjugate of a compstatin analogue, formulated both for intravitreal administration by injections directly into the eye, and systemic administration by subcutaneous injection, which is an injection into the tissue under the skin. We are also developing compounds targeting C3 for intravenous administration.

The following table summarizes key information about our ongoing clinical programs:

Program	Clinical Trials	Trial Participants	Estimated Timeline
Intravitreal pegcetacoplan			
GA	Phase 3 trials (DERBY/OAKS)	Patients with GA	Complete enrollment 1H 2020; top-line data mid-2021
Subcutaneous pegcetacoplan			
PNH	Phase 3 trial (PEGASUS)	Eculizumab-treated patients with PNH	Top-line data reported January 2020; 48 week data by 2H 2020
	Phase 3 trial (PRINCE)	Treatment-naïve patients with PNH	Complete enrollment 1H 2020; top-line data 1Q 2021
CAD	Phase 2 trial	Patients with CAD	Plans to be announced 1H 2020
C3G	Phase 2 trial	Patients with glomerular diseases with complement involvement	Plans to be announced 1H 2020
Intravenous C3 inhibition			
Gene therapies	Phase 1 trial	Healthy patients	Plans to be announced 2020

Intravitreal Pegcetacoplan

We are developing pegcetacoplan to be injected intravitreally as a monotherapy for patients with ophthalmological indications, including geographic atrophy, or GA. 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 July 2018, we received fast track designation from the FDA for pegcetacoplan in GA.

Our ongoing Phase 3 clinical program in GA consists of two 600-patient prospective, multicenter, randomized, double-masked, sham-injection controlled trials (DERBY and OAKS) at 200 sites worldwide to assess the efficacy and safety of multiple intravitreal injections of pegcetacoplan in patients with GA. Patients in each Phase 3 trial receive a dose of 15 mg of pegcetacoplan injected intravitreally in a 0.1 cc volume, monthly or every other month for 24 months. In the sham-injection cohorts, patients receive a simulated injection. As with our Phase 2 clinical trial, the primary endpoint of each trial is the change in total area of GA lesions in the study eye from baseline to month 12 compared to sham. The measurements of change will be analyzed at 12 months (primary endpoint) and 24 months. We dosed the first patient in the Phase 3 trials in September 2018. We expect that both trials will be fully enrolled by the end of the first half of 2020 and that we will announce data from these trials in mid-2021.

Subcutaneous Pegcetacoplan

PNH

We are developing pegcetacoplan to be injected subcutaneously as a monotherapy for patients with PNH. 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 therapies currently approved for the treatment of PNH, eculizumab (Soliris) and ravulizumab (Ultomiris), both of which are marketed by Alexion Pharmaceuticals, Inc., or Alexion, inhibit the complement system by targeting C5, a protein that is downstream from C3 in the complement cascade. Retrospective studies have reported that, even when treated with eculizumab, up to 70% of people with PNH have low hemoglobin levels and up to 36% require one or more transfusions a year. Based on prevalence data published in an abstract in a peer-reviewed journal, we estimate that there are approximately 15,000 patients with PNH worldwide.

If our clinical development of pegcetacoplan for PNH is successful, we believe that pegcetacoplan could be a best-in-class therapy for PNH, differentiated by mechanism, and that pegcetacoplan has the potential to significantly increase the quality of life of patients with PNH as compared to the current standard of care.

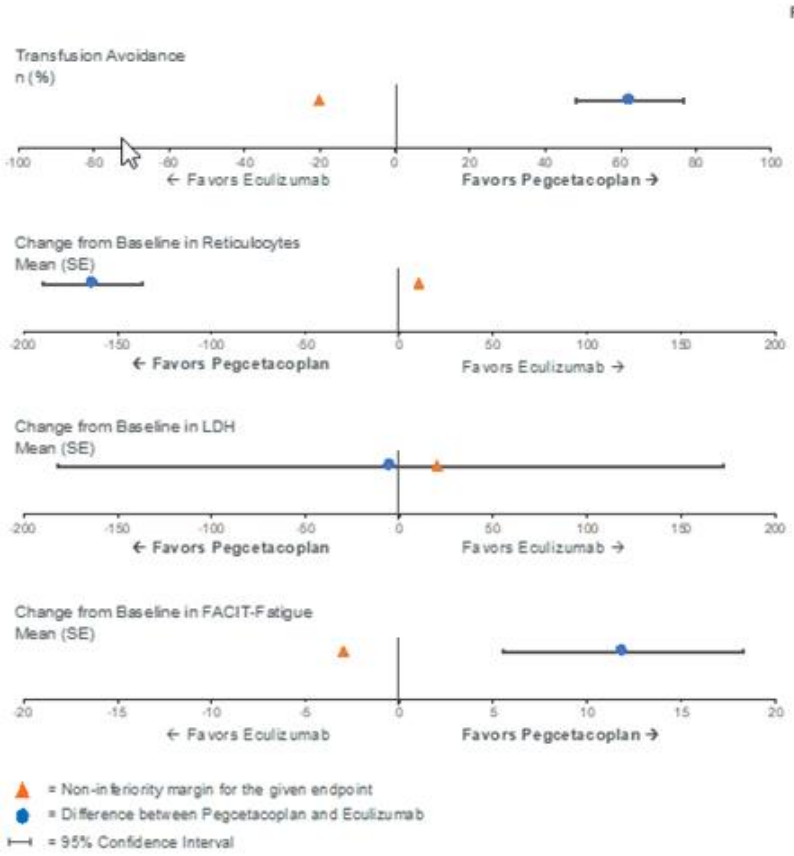
We initiated the Phase 3 PEGASUS trial in June 2018. The PEGASUS trial, is an 80-patient randomized head-to-head trial comparing pegcetacoplan monotherapy to eculizumab monotherapy in patients with PNH currently on treatment with eculizumab who have a hemoglobin level of less than 10.5 g/dL, regardless of eculizumab dose or transfusion history. The primary efficacy of the trial is the change in hemoglobin level from baseline at week 16.

The treatment period of the PEGASUS trial consists of three parts: a four-week run-in period, a 16-week randomized treatment period and a 32-week open-label pegcetacoplan only period. During the run-in period, all patients receive twice-weekly subcutaneous doses of 1,080 mg of pegcetacoplan in addition to patients' then current dose of eculizumab. The run-in period was designed to provide patients with sufficient plasma concentration of pegcetacoplan to provide for what we expected to be adequate complement inhibition before withdrawing eculizumab. Following completion of the run-in period, patients received either 1,080 mg of pegcetacoplan twice per week or their current dose of eculizumab through the duration of the 16-week randomized treatment period. Following completion of the randomized treatment period with either pegcetacoplan monotherapy or eculizumab monotherapy, all 80 patients had the option to receive pegcetacoplan monotherapy for 32 weeks in an open-label treatment period.

In January 2020, we announced top-line data from the PEGASUS trial that showed that pegcetacoplan met the trial's primary efficacy endpoint, demonstrating superiority to eculizumab with a statistically significant improvement in adjusted means of 3.8 g/dL of hemoglobin at week 16 ($p < 0.0001$). At week 16, pegcetacoplan-treated patients ($n = 41$) had an adjusted mean hemoglobin increase of 2.4 g/dL from a baseline of 8.7 g/dL, compared to eculizumab-treated patients ($n = 39$) who had a change of -1.5 g/dL from a baseline of 8.7 g/dL.

Additionally, pegcetacoplan showed promising results in key secondary endpoints. Pegcetacoplan met non-inferiority on transfusion avoidance and absolute reticulocyte count. Pegcetacoplan did not meet non-inferiority to eculizumab on mean LDH levels, which we believe is primarily due to the small number of eculizumab-treated patients who completed the 16 week randomized treatment period without transfusions. Pegcetacoplan showed positive trends on LDH and fatigue as measured by the FACIT-fatigue score.

The following table summarizes the reported results from the key secondary endpoints of the PEGASUS trial.



LDH = Lactate Dehydrogenase. FACIT = Functional Assessment of Chronic Illness Therapy. Mean (SE) = Adjusted means (SE) are based on the mixed model repeated measures (MMRM) analysis. CI = Confidence Interval. SE = Standard Error.

Key Secondary Endpoints analyses are based on pre-specified Non-Inferiority Margins. Non-inferiority is achieved if the LCL or UCL of the 95% CI of the treatment difference meets the pre-specified margin.

*Not tested: As LDH did not achieve non-inferiority, no other endpoints were tested.

The statistical analysis plan for the PEGASUS trial provided for use of the mixed model—repeated measures (MMRM) method. To avoid the effect of transfusions in hemoglobin levels during the 16-week randomization period of the trial, if a patient received a transfusion during the 16-week randomization period, any measurements after the first transfusion were censored from the data used in the MMRM analysis. The treatment effects using observed data from the trial, which included all post-transfusion measurements, were consistent with and supportive of the reported results from the MMRM analysis.

In the PEGASUS trial, the safety profile of pegcetacoplan was comparable to eculizumab. Seven of 41 patients (17.1%) in the pegcetacoplan group experienced a serious adverse event, or SAE, and 6 of 39 patients (15.4%) in the eculizumab group experienced SAEs. No cases of meningitis and no deaths were reported in either treatment group. The most common adverse events reported during the 16-week, randomized, controlled treatment period in the pegcetacoplan and eculizumab groups, respectively, were injection site reactions (36.6% vs. 2.6%), diarrhea (22.0% vs. 0%), headache (7.3% vs. 20.5%) and fatigue (4.9% vs. 15.4%). Another common adverse event was hemolysis, which was reported in four patients in the pegcetacoplan group (9.8%) and nine patients in the eculizumab group (23.1%). This led to the three discontinuations in pegcetacoplan group.

All patients who completed the randomization period in both groups (77/80) entered the 32-week open-label pegcetacoplan treatment period. We plan to present detailed 16-week results from the PEGASUS trial at a future scientific meeting and expect to report 48-week topline data in the second half of 2020.

We initiated the Phase 3 PRINCE trial in September 2019. The PRINCE trial is a 54-patient randomized, multicenter, open-label trial to evaluate the efficacy of pegcetacoplan in treatment-naïve patients. The primary endpoints are avoidance of a greater than 1 g/dL decrease in hemoglobin level from baseline in the absence of transfusion through week 26 and reduction in lactate dehydrogenase (LDH) level from baseline to week 26, in patients with PNH who are currently not being treated with complement inhibitors. Secondary endpoints include hemoglobin response (defined as an increase in hemoglobin levels greater than or equal to 1 g/dL), change in absolute reticulocyte count, change in hemoglobin levels, number of packed red blood cells transfused, change in FACIT score, hemoglobin normalization and LDH normalization. We expect to complete enrollment in this trial in the first half of 2020 and to present top-line data in the first quarter of 2021.

We intend to meet with regulatory agencies in the first half of 2020 to discuss what information is required to support regulatory submissions of an NDA and an MAA for pegcetacoplan in PNH. The FDA has advised us that, for the approval of a new treatment for PNH, hemoglobin stabilization in conjunction with change in transfusion dependence constitute accepted clinical benefit, but that a rise in hemoglobin levels may not translate to clinical benefit in patients who entered the trial with high hemoglobin levels, such as permitted by the inclusion criteria of the PEGASUS trial, and who do not require transfusions. We believe that the data from the PEGASUS trial support a finding of clinical benefit. As clinical data is susceptible to varying interpretations and analyses, we will need to discuss our data with the FDA, European Medicines Agency, or EMA, and other regulatory agencies before we can determine our next steps.

In April 2014, we received orphan drug designation from the FDA for pegcetacoplan for PNH. In February 2019 we received fast track designation from the FDA for pegcetacoplan for patients with PNH, which superseded the fast track designation we received in December 2016 for pegcetacoplan for the subset of patients with PNH who continue to require transfusions despite receiving therapy with eculizumab.

CAD

We are developing pegcetacoplan to be injected subcutaneously as a monotherapy for patients with CAD. In March 2018, we initiated a Phase 2 clinical trial of pegcetacoplan administered by subcutaneous injection in patients with CAD. CAD is a severe, chronic rare autoimmune disorder caused by pathogenic immunoglobulin M antibodies that react with red blood cells at body temperatures below 30^{o}C and leads to clumping, or agglutination, of red blood cells. Agglutinated red blood cells activate the complement system leading to destruction of the red blood cells. The disease is often characterized by chronic anemia, severe fatigue, and an increased risk of life-threatening events such as stroke. There are an estimated 10,000 CAD patients across the United States and Europe. There are currently no approved therapies for CAD.

In June 2019, we announced interim data from the Phase 2 trial. As of June 15, 2019, we had enrolled 13 patients with CAD in the Phase 2 trial, of which 10 patients had been treated for at least 168 days. In this clinical trial, treatment with pegcetacoplan reduced extravascular hemolysis, measured by increased hemoglobin levels and reduced reticulocytes and bilirubin levels, and intravascular hemolysis measured by reduced LDH in patients with CAD. We intend to disclose our plans and timing for further clinical development of pegcetacoplan for patients with CAD in the first half of 2020.

C3G

We are currently conducting a Phase 2 clinical trial of pegcetacoplan in C3G and other glomerular diseases in which complement has been implicated including IgA nephropathy, primary membranous nephropathy and lupus nephritis. We initiated this trial in the first quarter of 2018. The primary endpoint is change from baseline in proteinuria at week 48 as quantified by urine protein-to-creatinine ratio, or uPCR. Secondary endpoints include analysis of serum C3 and estimated glomerular filtration rate.

In November 2019, we presented preliminary data from six patients in the C3G cohort of the Phase 2 trial. The data showed that pegcetacoplan may have the potential to target the underlying disease process of C3G. In the six patients, the preliminary data showed a downward trend in mean proteinuria as measured by uPCR. Mean (SE) uPCR decreased from 2.03 (0.46) mg/mg to 1.05 (0.23) mg/mg at study day 84 (normal range < 0.200 mg/mg), and a corresponding normalization of mean serum albumin was observed. Serum C3 levels also increased in all six of these patients. No serious adverse events and no discontinuations due to adverse events were reported in patients with C3G.

In December 2018, we received orphan drug designation from the FDA for the treatment of C3G. We intend to disclose our plans and timing for further clinical development of pegcetacoplan for patients with C3G in the first half of 2020.

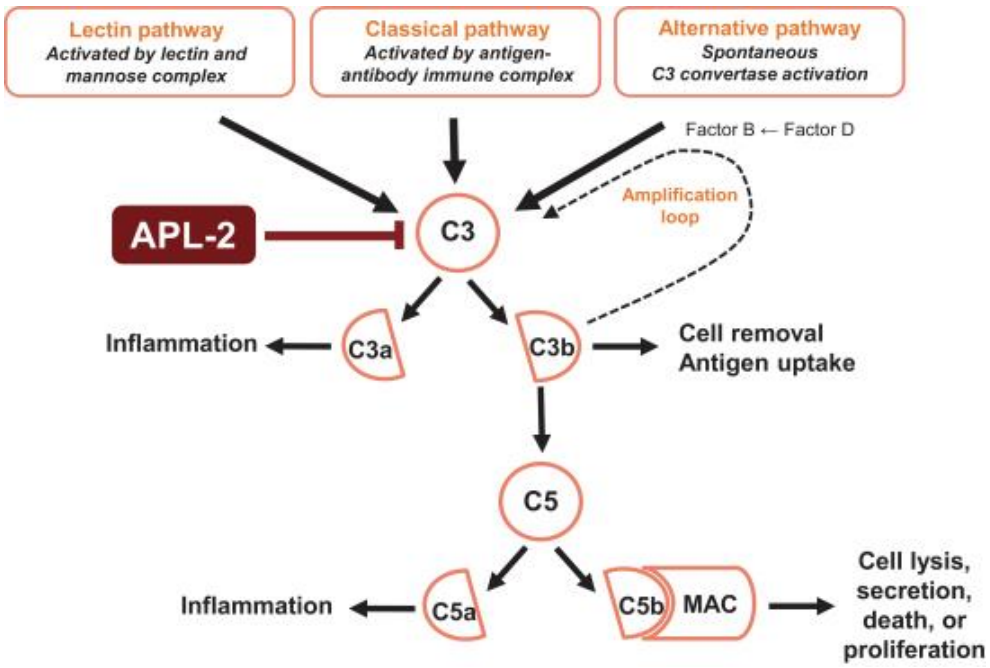
Intravenous C3 Inhibition

We are developing compounds targeting C3 for intravenous administration. In particular, we are developing APL-9 for the prevention of complement immune system activation coincident with adeno-associated virus, or AAV, vector administration for gene therapies and other indications. APL-9 is a second generation C3 modulator and is designed to be intravenously administered for acute use.

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 B or 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 pegcetacoplan 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, CAD, and C3G. We believe that pegcetacoplan 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.

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. We hold worldwide commercialization rights to pegcetacoplan and have the flexibility to develop and potentially commercialize pegcetacoplan ourselves or alternatively to seek to enter into collaborations with industry partners. To achieve our goals, we are pursuing the following strategies:

- ***Complete Phase 3 clinical development of intravitreal pegcetacoplan in GA***. We are developing pegcetacoplan as monotherapy for GA, administered by intravitreal injections. We are conducting two 600-patient Phase 3 clinical trials of pegcetacoplan in GA to assess the efficacy and safety of multiple intravitreal injections of pegcetacoplan in patients with GA. We expect to have fully enrolled both trials by the end of the first half of 2020 and that we will announce data from these trials in mid-2021.
- ***Prepare for regulatory submission and commercialization of subcutaneous pegcetacoplan in PNH.*** We are developing pegcetacoplan as monotherapy for patients with PNH, administered by subcutaneous injection. In January 2020, we announced top-line data from the Phase 3 PEGASUS trial that showed that pegcetacoplan met the trial's primary efficacy endpoint, demonstrating superiority to eculizumab with a statistically significant improvement in adjusted means of 3.8 g/dL of hemoglobin at week 16 ($p < 0.0001$) and showed promising results in key secondary endpoints, including transfusion avoidance and absolute reticulocyte count. We plan to present detailed 16-week results from the PEGASUS trial at a future scientific meeting and expect to report 48-week topline data in the second half of 2020**.** We expect to complete enrollment in the PRINCE trial in the first half of 2020 and to present top-line data in the first quarter of 2021. We intend to meet with and discuss our data with the FDA, EMA and other regulatory agencies in the first half of 2020 to discuss what information is required to support regulatory submissions of an NDA and an MAA for pegcetacoplan in PNH.
- ***Continue clinical development of subcutaneous pegcetacoplan in other indications, including CAD and C3G.*** We are developing pegcetacoplan for patients with CAD and C3G, administered by subcutaneous injection. We intend to disclose our plans and timing for further clinical development of pegcetacoplan for patients with CAD and C3G in the first half of 2020.
- ***Continue development of our intravenous C3 inhibition program and expand our pipeline***. We are developing compounds targeting C3 for intravenous administration. In particular, we are developing APL-9 for the prevention of complement immune system activation coincident with AAV vector administration for gene therapies. In addition, we believe that our core expertise in complement inhibition and our understanding of immunology and the role of the complement system in disease, positions us to continue to develop a pipeline of treatments for a broad range of autoimmune and inflammatory diseases with pegcetacoplan and additional new product candidates.

Intravitreal pegcetacoplan

Geographic Atrophy

Background

GA is a type of advanced age-related macular degeneration, or AMD. According to the Brightfocus Foundation, over ten million people in the United States have some form of 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 and then to an advanced stage associated with progressive and often severe vision loss which may be characterized as either GA or wet AMD. 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. 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 pegcetacoplan 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 pegcetacoplan may control complement activation in the retinal environment to return to its quiescent state. We do not believe that selective inhibitors of the alternative pathway, which would only partially block 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, therapies in development for GA. For instance, Zimura, a C5 inhibitor being developed by Iveric Bio, is in Phase 2/3 trials.

Benefits of Our Approach

We believe pegcetacoplan, with its inhibition of complement activation at the level of C3 in the retinal environment, may provide the following benefits:

- *Prevention or reduction of the rate of retinal cell death progression*. We believe pegcetacoplan may mitigate or prevent retinal cell death in GA. In our Phase 2 trial of pegcetacoplan in patients with GA, treatment with pegcetacoplan 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.* Pegcetacoplan, 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 our Phase 2 trial, that the activity of pegcetacoplan does not depend upon the activation of any particular complement pathway.

Clinical Development

We initiated Phase 3 clinical trials of pegcetacoplan in patients with GA following completion of a Phase 2 clinical trial in patients with GA, which we refer to as the FILLY trial. In August 2017, we completed the primary endpoint analysis for the 12-month treatment period for the Phase 2 FILLY trial and in February 2018 we completed the analysis of data from the six-month monitoring period from that trial. Prior to the FILLY trial, we completed a Phase 1 clinical trial of pegcetacoplan in patients with wet AMD in 2016. In July 2018, we received fast track designation from the FDA for pegcetacoplan in GA.

Phase 3 Clinical Trials

Our Phase 3 clinical program for the development of intravitreal pegcetacoplan is ongoing. The Phase 3 program in GA consists of two 600-patient prospective, multicenter, randomized, double-masked, sham-injection controlled trials to assess the efficacy and safety of multiple intravitreal injections of pegcetacoplan in patients with GA, with the goal of enrolling a total of 1,200 patients across approximately 200 sites worldwide. We refer to these trials as the DERBY and OAKS trials. We dosed the first patient in our Phase 3 trials in September 2018. We believe that both trials will be fully enrolled by the end of the first half of 2020 and that we will announce data from these trials in mid-2021.

Patients in each Phase 3 trial receive a dose of 15 mg of pegcetacoplan injected intravitreally in a 0.1 cc volume, monthly or every other month for 24 months. In the sham-injection cohorts, patients receive a simulated injection. As with our Phase 2 clinical trial, the primary endpoint of each trial is the change in total area of GA lesions in the study eye from baseline to month 12 compared to sham. The measurements of change in lesion size will be analyzed at 12 months (primary endpoint) and 24 months. We 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 pegcetacoplan along with anti-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 FILLY trial, we believe that pegcetacoplan 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 a second assessment after 24 months of treatment. This design is in line with the recommendations of the FDA and the EMA.

We are using a liquid formulation of pegcetacoplan in our Phase 3 trials instead of the freeze-dried formulation that we used in the Phase 2 FILLY trial, which we believe may reduce the incidence of endophthalmitis.

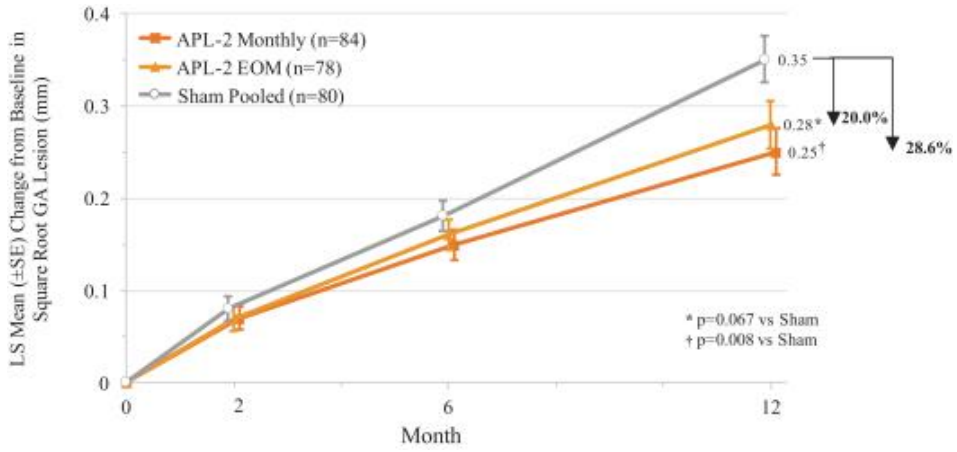
In October 2018, we announced that we voluntarily implemented a pause in dosing in our Phase 3 clinical trials in patients with GA due to observed cases of non-infectious inflammation in patients treated from a single manufacturing lot of pegcetacoplan intravitreal drug product. Four patients in the Phase 3 GA program were treated with pegcetacoplan from this manufacturing lot and each patient developed non-infectious inflammation. Inflammation in all patients completely resolved. We reviewed these events with the data safety monitoring board for our GA trials, conducted a series of non-human studies and introduced improvements to the manufacturing process. Based on these efforts, we believe that the source of inflammation resided in a contaminant or impurity in the active pharmaceutical ingredient. We resumed the trials in March 2019.

Phase 2 Clinical Trial

In the third quarter of 2015, we initiated a Phase 2 multicenter, randomized, single-masked, sham-controlled clinical trial of pegcetacoplan in patients with GA, which we refer to as the FILLY trial, 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 pegcetacoplan monthly, pegcetacoplan every other month, sham injection monthly or sham injection every other month. Patients in the pegcetacoplan arms received a dose of 15 mg of pegcetacoplan 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, 12 and 18.

We conducted this trial to assess the safety, tolerability, pharmacokinetics, or PK, and evidence of activity of multiple intravitreal injections of pegcetacoplan 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 pegcetacoplan every month, 78 patients receiving administration of pegcetacoplan 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.

We announced 12-month results of the Phase 2 trial in August 2017. After 12 months, patients treated monthly with pegcetacoplan 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.

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 who received monthly pegcetacoplan, and for whom images were available at 12 and 18 months 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 pegcetacoplan 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 pegcetacoplan 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 pegcetacoplan showed a 16% reduction in the growth rate of lesions over the full 18-month period compared to sham.

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.

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 pegcetacoplan 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 pegcetacoplan every month and seven patients (9%) receiving administration of pegcetacoplan 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 pegcetacoplan 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.

Phase 1b/2 Clinical Trial in Wet AMD

We conducted a Phase 1b/2, multi-center, open label clinical trial to evaluate the safety of intravitreal pegcetacoplan therapy when administered in parallel with anti-VEGF treatments in patients with wet AMD in the study eye in the second quarter of 2018. As with our Phase 3 program in GA, we voluntarily implemented a pause in our Phase 1b/2 trial of pegcetacoplan in patients with wet AMD in October 2018. We decided to discontinue the Phase 1b/2 trial of pegcetacoplan in patients with wet AMD.

Phase 1 Clinical Trial in Low Vision Geography Atrophy

We are conducting a Phase 1b clinical trial to evaluate the safety of monthly intravitreal treatments with pegcetacoplan in up to 12 patients with GA secondary to AMD and with low vision, which we initiated in September 2018.

Phase 1 Clinical Trial

We conducted a Phase 1 open label, ascending single-dose clinical trial of pegcetacoplan 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 pegcetacoplan. In this trial, patients received a single dose of pegcetacoplan by intravitreal injection followed by 113 days of monitoring. We enrolled eighteen patients in the trial, in three cohorts, at doses of 5 mg (3 patients), 10 mg (3 patients) and 20 mg (12 patients) of pegcetacoplan. Pegcetacoplan 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 trial.

Preclinical Studies

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

Subcutaneous Pegcetacoplan

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

Eculizumab, marketed as Soliris, and ravulizumab, marketed as Ultomiris, both by Alexion, are the only therapies that have been approved for the treatment of PNH. Alexion has reported that eculizumab had worldwide sales of more than $3.6 billion in 2018 for its three approved indications, PNH, atypical hemolytic-uremic syndrome, or aHUS, and refractory myasthenia gravis in ACHR+ 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. Ravulizumab is administered intravenously every weeks and subcutaneously once per week and is designed to have a longer half-life and greater inhibition of C5 than eculizumab. Ravulizumab was tested in two Phase 3 non-inferiority trials with Soliris and was found to be non-inferior.

Retrospective studies have reported that up to 70% of patients with PNH who are on treatment with eculizumab remained anemic and up to 36% of patients on eculizumab continued to require at least one transfusion per year. In these studies, 100% of patients with PNH on eculizumab showed evidence of C3-related opsonization on their red blood cells. We believe that uncontrolled extravascular hemolysis is responsible in part for these continuing complications.

Benefits of Our Approach

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

- *Prevention of intravascular hemolysis and its consequences*. Pegcetacoplan may prevent the formation of the membrane attack complex on blood cells 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*. Pegcetacoplan may prevent C3b opsonization, on blood cells, and may thereby prevent extravascular hemolysis, further reducing anemia and transfusion dependency in patients with PNH.
- *Ease and convenience of use*. We believe that the ability to self-administer pegcetacoplan by subcutaneous injection on a regular basis could improve the quality of life for patients with PNH by eliminating the need to travel to a health care facility for intravenous treatment.

Clinical Development

Our clinical development program is guided by a planned commercial switch-over strategy for pegcetacoplan. Under this strategy, if we are able to obtain marketing approval for pegcetacoplan for PNH, we plan to allow PNH patients on treatment with eculizumab to assess the benefit of pegcetacoplan in co-treatment with eculizumab for a limited time, before deciding to switch to pegcetacoplan monotherapy or to revert to eculizumab monotherapy.

Phase 3 Clinical Trial - PEGASUS

We initiated the Phase 3 PEGASUS trial in patients in June 2018. The PEGASUS trial is an 80-patient randomized head-to-head trial comparing pegcetacoplan monotherapy to eculizumab monotherapy in patients with PNH currently on treatment with eculizumab who have a hemoglobin level of less than 10.5 g/dL, regarding of eculizumab dose or transfusion history. The primary efficacy endpoint of the trial is the change in hemoglobin level from baseline at week 16. The PEGASUS trial was fully enrolled in June 2019. The treatment period of the trial consists of three parts: a four-week run-in period, a 16-week randomized treatment period and a 32-week open-label pegcetacoplan only period. During the run-in period, all patients receive twice-weekly subcutaneous doses of 1,080 mg of pegcetacoplan in addition to patients' then current dose of eculizumab. The run-in period is designed to provide patients with sufficient plasma concentration of pegcetacoplan to provide for what we expected to be adequate complement inhibition before withdrawing eculizumab. Following completion of the run-in period, patients received either 1,080 mg of pegcetacoplan twice per week or their current dose of eculizumab through the duration of the 16-week randomized treatment period. Following completion of the randomized treatment period with either pegcetacoplan monotherapy or eculizumab monotherapy, all 80 patients had the option to receive pegcetacoplan monotherapy for 32 weeks in an open-label treatment period.

In January 2020, we announced top-line data from the PEGASUS trial that showed that pegcetacoplan met the primary efficacy endpoint, demonstrating superiority to eculizumab with a statistically significant improvement in adjusted means of 3.8 g/dL of hemoglobin at week 16 ($p < 0.0001$). At week 16, pegcetacoplan-treated patients ($n = 41$) had an adjusted mean hemoglobin increase of 2.4 g/dL from a baseline of 8.7 g/dL, compared to eculizumab-treated patients ($n = 39$) who had a change of -1.5 g/dL from a baseline of 8.7 g/dL. Additionally, pegcetacoplan showed promising results in key secondary endpoints. Pegcetacoplan met non-inferiority on transfusion avoidance and absolute reticulocyte count. Pegcetacoplan did not meet pre-specified criteria for non-inferiority on mean LDH levels. Pegcetacoplan showed positive trends on LDH and fatigue as measured by the FACIT-fatigue score. The statistical analysis plan for the PEGASUS trial provided for use of the mixed model—repeated measures (MMRM) method. To avoid the effect of transfusions in hemoglobin levels during the 16-week randomization period of the trial, if a patient received a transfusion during the 16-week randomization period, any measurements after the first transfusion were censored from the data used in the MMRM analysis. The treatment effects using observed data from the trial, which included all post-transfusion measurements, were consistent with and supportive of the reported results from the MMRM analysis.

In the trial, the safety profile of pegcetacoplan was comparable to eculizumab. Seven of 41 patients (17.1%) in the pegcetacoplan group experienced a serious adverse event, or SAE, and six of 39 patients (15.4%) in the eculizumab group experienced SAEs. No cases of meningitis and no deaths were reported in either treatment group. The most common adverse events reported during the 16-week, randomized, controlled treatment period in the pegcetacoplan and eculizumab groups, respectively, were injection site reactions (36.6% vs. 2.6%), diarrhea (22.0% vs. 0%), headache (7.3% vs. 20.5%) and fatigue (4.9% vs. 15.4%). Another common adverse event was hemolysis, which was reported in four patients in the pegcetacoplan group (9.8%) and nine patients in the eculizumab group (23.1%). This led to the three discontinuations in pegcetacoplan group.

All patients who completed the randomization period in both groups (77/80) entered the 32-week open-label pegcetacoplan treatment period.

Phase 3 Clinical Trial – PRINCE

We initiated the Phase 3 PRINCE trial in September 2019. The PRINCE trial is a 54-patient randomized, multicenter, open-label trial to evaluate the efficacy of pegcetacoplan in treatment-naïve patients. The primary endpoints are avoidance of a greater than 1 g/dL decrease in hemoglobin level from baseline in the absence of transfusion through week 26 and reduction in lactate dehydrogenase (LDH) level from baseline to week 26, in patients with PNH who are currently not being treated with complement inhibitors. Secondary endpoints include hemoglobin response (defined as an increase in hemoglobin levels greater than or equal to 1 g/dL), change in absolute reticulocyte count, change in hemoglobin levels, number of packed red blood cells transfused, change in FACIT score, hemoglobin normalization and LDH normalization. We expect to complete enrollment in this trial in the first half of 2020 and to present top-line data in the first quarter of 2021.

Phase 1b Clinical Trials – PHAROAH and PADDOCK

We have conducted two clinical trials of pegcetacoplan as part of our PNH program: a Phase 1b clinical trial (PHAROAH) in patients with PNH being treated with eculizumab, which has concluded, and an on-going Phase 1b clinical trial (PADDOCK) in

treatment-naïve patients, which is ongoing. These trials were designed to assess safety and tolerability and whether pegcetacoplan has the potential to control PNH. In these trials, we measured 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 also measured 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.

PHAROAH was a Phase 1b open-label, single and multiple ascending dose clinical trial of pegcetacoplan in patients with PNH who are receiving eculizumab, conducted at multiple clinical sites in the United States. In the PHAROAH trial, doses of pegcetacoplan were administered by subcutaneous injection to patients with PNH who were concurrently being treated with eculizumab at varying doses according to the treating physicians' recommendations. We treated a total of nine patients in the PHAROAH trial. Pegcetacoplan was 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 pegcetacoplan. We initiated this trial in February 2015 and the last patient transitioned in October 2018 into a long-term extension study that we are conducting.

PADDOCK is a Phase 1b open-label clinical trial of pegcetacoplan in treatment-naïve patients with PNH that we initiated in December 2015 and are conducting this trial at multiple clinical sites outside of the United States. In the PADDOCK trial, doses of pegcetacoplan were initially administered by subcutaneous injection during the treatment period. We have treated a total of 22 patients in the PADDOCK trial, of which 15 are currently enrolled in the long-term extension study. As of February 24, 2020, pegcetacoplan had been generally well tolerated in these patients with 13 serious adverse events reported across seven patients. Only one of these serious adverse events was noted as possibly related to administration of pegcetacoplan.

In both Phase 1b trials, patients treated with pegcetacoplan experienced reductions in LDH levels, and improved hemoglobin levels. Furthermore, we have observed lower reticulocyte counts in patients treated with pegcetacoplan, 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.

Long-Term Extension Study

We are conducting a long-term extension study of pegcetacoplan in patients with PNH who participated in previous clinical trials with pegcetacoplan. This study is an open label, non-randomized, multi-center study to evaluate the long-term safety and efficacy of pegcetacoplan in the treatment of PNH with dosing for a longer period and at doses of 1,080 mg given either twice a week or every three days. The study is being carried out with fifteen patients who were enrolled in our Phase 1b studies. We expect to continue the extension study until pegcetacoplan becomes commercially available in the subject's participating country, or until the development program for pegcetacoplan in subjects with PNH is terminated.

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 pegcetacoplan in a total of 55 healthy volunteers. We conducted the trials at a single site in Australia to assess the safety, tolerability, PK and pharmacodynamics, or PD of pegcetacoplan. Pegcetacoplan was well tolerated in both trials with no serious adverse events reported, and the PK of pegcetacoplan in humans was in line with our expectations derived from preclinical data, with little inter-subject variability observed. In both trials, we observed a dose-dependent increase in C3 that is indicative of pegcetacoplan binding to C3.

Supporting Clinical Trials and Studies

We conducted a Phase 1 trial to assess the safety and tolerability of pegcetacoplan 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. No significant difference in PK parameters was noted.

We conducted a Phase 1 trial to determine the safety, PK and PD of twice-weekly and once-weekly subcutaneous administration of pegcetacoplan in healthy volunteers. We are evaluating 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 conducted a Phase 1 trial to determine the safety, PK and PD of pegcetacoplan in healthy volunteers of Japanese descent. We intend to evaluate whether pegcetacoplan will have comparable PK and PD profiles in this population. No significant difference in PK parameters was noted.

Preclinical Studies

We have conducted numerous preclinical studies of pegcetacoplan in animals and in laboratory samples to assess the safety of pegcetacoplan, including repeat-dose subcutaneous and intravenous toxicity studies of pegcetacoplan 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 pegcetacoplan 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, pegcetacoplan 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.

Safety

In all trials of pegcetacoplan 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. As of July 10, 2019, in our clinical trials of pegcetacoplan using subcutaneous administration, in patients or healthy volunteers, a total of 49 serious adverse events had been reported in 24 of the 192 subjects. Of these 49 serious adverse events, 5 were considered to be at least possibly related to study medication by the investigator. None of these indicated any unexpected safety concerns.

Regulatory Matters

We intend to meet with regulatory agencies in the first half of 2020 to discuss what information is required to support regulatory submissions of an NDA and an MAA for pegcetacoplan in PNH. The FDA has advised us that, for the approval of a new treatment for PNH, hemoglobin stabilization in conjunction with change in transfusion dependence constitute accepted clinical benefit, but that a rise in hemoglobin levels may not translate to clinical benefit in patients who entered the trial with high hemoglobin levels, such as permitted by the inclusion criteria of the PEGASUS trial, and who do not require transfusions. We believe that the data from the PEGASUS trial support a finding of clinical benefit. As clinical data is susceptible to varying interpretations and analyses, we will need to discuss our data with the FDA, EMA and other regulatory agencies before we can determine our next steps.

In July 2014, we submitted an IND to the FDA for the clinical development of pegcetacoplan for the treatment of PNH. In April 2014, we received orphan drug designation from the FDA for pegcetacoplan for PNH. In February 2019 we received fast track designation from the FDA for pegcetacoplan for patients with PNH, which superseded the fast track designation we received in December 2016 for pegcetacoplan for the subset of patients with PNH who continue to require transfusions despite receiving therapy with eculizumab.

Cold Agglutinin Disease

Cold agglutinin disease, or CAD, is a severe, chronic rare autoimmune disorder caused by pathogenic immunoglobulin M antibodies that react with red blood cells at body temperatures below 30ºC and leads to agglutination of red blood cells. Like other autoimmune hemolytic anemias, CAD is characterized by autoantibody-initiated premature destruction of red blood cells, chronic anemia, severe fatigue, and an increased risk of life-threatening events such as stroke. There are an estimated 10,000 CAD patients across the United States and Europe. The complement system plays a major role in red blood cell destruction in CAD 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 pegcetacoplan as a monotherapy for CAD. In March 2018, we initiated a Phase 2 open label clinical trial of pegcetacoplan administered by subcutaneous injection in patients with CAD, which we refer to as the PLAUDIT trial. In the PLAUDIT trial, doses of pegcetacoplan were initially administered by subcutaneous injection during the treatment period, followed by a long-term extension period. We have treated a total of 24 patients with CAD in the PLAUDIT trial, of which 13 are currently enrolled. In December 2018, we announced interim data for the Phase 2 trial at the ASH Conference and further interim data at the European Hematology Association Congress in June 2019. We observed that in the 10 patients with CAD who reached day 168:

- 70% showed a Hb increase of ≥ 2 g/dL, 40% had normalized Hb (≥ 12.0 g/dL) and 80% had Hb ≥ 11.0 g/dL at Day 168.
- Mean Hb increased from 8.9 g/dL at baseline to 11.2 g/dL at Day 168, a 2.4 g/dL increase (normal Hb is 12 - 16 g/dL).
- Mean Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue Score increased from 29.4 at baseline to 39.1 at Day 168, an improvement of 9.7 points, where a clinically significant increase is 3 or more points.
- Mean absolute reticulocyte count (ARC) decreased from 138.6 X 10^9/L at baseline to 63.6 X 10^9/L at Day 168 (normal ARC is 30 - 100 X 10^9/L).
- Mean indirect bilirubin decreased from 1.9 mg/dL at baseline to 0.4 mg/dL at Day 168 (normal indirect bilirubin is 0.1 -0.75 mg/dL).
- Mean LDH decreased from 486.5 U/L at baseline to 183.2 U/L at Day 168 (normal LDH is 87 - 252 U/L).

As of December 31, 2019, pegcetacoplan had been generally well tolerated in these patients with 13 serious adverse events reported, across ten patients, of which all are considered unlikely to be related to administration of pegcetacoplan.

There is no FDA-approved drug therapy specifically for CAD. 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 patients with CAD, 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 have discussed our plans for clinical development in CAD with the FDA and other regulatory agencies and will incorporate their feedback. We intend to disclose our plans and timing for further clinical development of pegcetacoplan for patients with CAD in the first half of 2020.

C3 Glomerulopathy

C3 glomerulopathy, or C3G, is a disease in which complement activation is believed to play an important role in kidney injury. There are no medicines currently approved for C3G, a rare disease that leads to kidney failure within five to 10 years of diagnosis in approximately 50% of people. In C3G, a part of the immune system known as the complement cascade is overactive, which results in the excessive breakdown of a protein called C3. These C3 breakdown products become trapped in the glomeruli, the filtering units of the kidney, causing inflammation and tissue damage. Proteinuria, or loss of blood proteins (e.g. albumin) in the urine, is a common finding in people with C3G, and an indication that the disease is damaging the kidneys. Pegcetacoplan is designed to prevent C3 activation, and as such, we believe it has the potential to prevent further deposition of C3 activation products in the glomeruli, which may protect the kidney from further injury.

In February 2018, we initiated a Phase 2 clinical trial of pegcetacoplan in biopsy-proven C3G and other glomerular diseases in which complement has been implicated, including IgA nephropathy, primary membranous nephropathy and lupus nephritis to evaluate the safety and biologic activity of pegcetacoplan in patients with these glomerular diseases. Each patient will receive once daily subcutaneous infusions of up to 360 mg of pegcetacoplan for one year. The primary efficacy endpoint is the reduction in proteinuria from baseline to week 48 as quantified by uPCR. Based on the scientific literature as well as the underlying pathophysiology of the disease, we believe that a substantial change in proteinuria is reasonably likely to predict a clinical benefit in all four glomerular diseases. Secondary endpoints include analysis of serum C3 and estimated glomerular filtration rate. We reported preliminary data from six patients in the C3G cohort in November 2019.

In the data presented on six C3G patients treated with pegcetacoplan for 84 days, there was a downward trend in mean proteinuria as measured by uPCR. Mean (SE) uPCR decreased from 2.03 (0.46) mg/mg to 1.05 (0.23) mg/mg at study day 84 (normal range <0.200 mg/mg), a 48% reduction, and a corresponding normalization of mean serum albumin was observed. Serum C3 levels also increased in all six of these patients. No serious adverse events and no discontinuations due to adverse events were reported in individuals with C3G.

We met with the FDA in October 2017 in a pre-IND meeting and submitted an IND to the FDA in November 2017. In December 2018, we received orphan drug designation from the FDA for the treatment of C3G. We intend to disclose our plans and timing for further clinical development of pegcetacoplan for patients with C3G in the first half of 2020.

Intravenous C3 Inhibition

We are developing compounds targeting C3 for intravenous administration. In particular, we are developing APL-9 for the prevention of complement immune system activation coincident with AAV vector administration for gene therapies and other indications. APL-9 is a second generation C3 modulator and is designed to be intravenously administered for acute use.

We believe that targeted control of C3 may prevent the C3-mediated attack on AAV particles, yielding three important potential advantages. First, controlling C3 may significantly increase the efficiency of gene therapy delivery by protecting the AAV particles on their journey from the site of administration to the target tissue. This may reduce the amount of particles needed to be used in gene therapies. Second, control of C3 may minimize the formation of anti-AAV neutralizing antibodies that can complicate subsequent retreatment with the same AAV. Finally, by countering the rapid activation of C3 upon administration of AAV particles, control of C3 may prevent inflammatory reactions that can lead to significant organ damage.

We have conducted a single ascending dose Phase 1 randomized, double-blind, placebo-controlled clinical trials of APL-9 in 20 healthy volunteers to determine the safety, PK and PD of APL-9. In this trial, APL-9 was administered either as a single intravenous dose infused over 30 minutes or as a slow bolus intravenous loading dose to provide rapid pharmacological complement inhibition followed by a continuous intravenous infusion to maintain pharmacological levels of APL-9 for the desired duration. APL-9 demonstrated control of complement through modulation of C3 within one hour of administration, that lasted up to 12 hours after the end of the infusion. Multiple doses tested achieved complete suppression of the AH50 hemolytic activity. In this Phase I study, APL-9 was well tolerated with no serious adverse events reported. In the study, complement activity resumed shortly after the termination of the intravenous infusion.

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.

Pegcetacoplan and APL-9 are analogs 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 Pharmaceuticals, Inc., or Potentia, in September 2015. The intellectual property in-licensed under our two license agreements with Penn includes four U.S. patents and one pending U.S. patent application, 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 candidates, pegcetacoplan and APL-9, 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, 2019, we own a total of eleven U.S. patents and 23 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 pegcetacoplan, and/or to methods of treatment and dosing regimens for treating particular complement-dependent diseases. Patents in these families 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 pegcetacoplan. 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 pegcetacoplan, 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 product candidates, pegcetacoplan and APL-9, and specifically recite the active component.

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.

In 2018 we made payments of $375,000, net of a credit for the annual license maintenance payment, for the achievement of milestones under this agreement.

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.

In 2018 we made payments of $650,000, net of a credit for the annual license maintenance payment, for the achievement of milestones under this agreement.

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 by Novartis AG as a monotherapy or adjunctive therapy with LFG316, an anti-C5 monoclonal antibody, in Phase 2 clinical trials; Zimura, a C5 inhibitor being developed by Iveric bio (formerly known as Ophthotech Corporation) 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 therapies being developed by Alcon, Allegro Ophthalmics LLC, Allergan PLC, Cell Cure Neurosciences, Genentech, Hemera Biosciences, Ionis Pharmaceuticals, Inc., Janssen Research & Development, LLC, Regenerative Patch Technologies, Stealth BioTherapeutics Corp., Gyroscope Therapeutics, and BioTime, Inc. In October 2019 Alexion obtained an option to co-develop and commercialize elamipretide for certain indications, including geography atrophy, from Stealth BioTherapeutics. Stealth is evaluating elamipretide in a Phase 2 clinical trial in patients with GA.

PNH. The principal competitors for PNH, and possibly other indications in our hematology and nephrology programs are eculizumab (marketed as Soliris) and ravulizumab (marketed as Ultomiris), C5 complement inhibitors, developed and marketed by Alexion. Eculizumab and ravulizumab are the only drugs approved for the treatment of PNH. Alexion is developing danicopan, formerly ACHN-4471, an orally available complement factor D inhibitor, currently in Phase 2 clinical trials as a cotreatment or combination product with eculizumab, and next generation complement factor D inhibitors ACHN-5528 and ACHN-5548, which are in early clinical development. 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:

- AMY-101, a C3 complement inhibitor being developed by Amyndas Pharmaceuticals SA; cemdisiran, an RNAi therapeutic targeting C5 developed by Alnylam Pharmaceuticals, Inc. in early clinical trials; nomacopan, a small protein C5 complement inhibitor being developed by Akari Therapeutics, Plc. in Phase 2 clinical trials; BCX9930, a Factor D inhibitor being developed by BioCryst, currently in early clinical development; zilucoplan, a cyclic peptide C5 inhibitor

developed by Ra Pharmaceuticals, Inc., or Ra, currently in Phase 2 clinical trials, crovalimab, an anti-C5 antibody developed by Roche/Chugai, currently in Phase 2 clinical trials; pozelimab, an anti-C5 antibody developed by Regeneron, currently in Phase 2 clinical trials; and LNP-023, a Factor B inhibitor being developed by Novartis currently in Phase 2 clinical trials;

- 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
- Amgen is developing ABP959, a biosimilar for eculizumab that is in Phase 3 clinical development.

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

- sutimlimab, a C1s monoclonal antibody inhibitor, being developed by Sanofi, is in Phase 3 clinical trials;
- paraclisib, p P13K-8 inhibitor, being developed by Incyte, is in Phase 2 clinical trials; and
- KZR-616, a proteasome inhibitor, being developed by Kezar Lifesciences, is in Phase 2 clinical trials.

C3 Glomerulopathy. There are no currently marketed drug treatments for C3 glomerulopathy, but there are currently treatments in development for C3G including narsoplimab (OMS721), a human monoclonal antibody to mannose-binding lectin-associated serine protease-2 (MASP-2) that blocks the lectin pathway, being developed by Omeros Corp., which is in Phase 2 clinical trials; avacopan, an oral C5aR-inhibitor developed by ChemoCentryx, Inc., which is in Phase 2 clinical trials; LNP023, a complement factor inhibitor being developed by Novartis, for C3 glomerulopathy which is in Phase 2 clinical trials; and danicopan, being developed by Alexion for C3G, which is in Phase 2 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. The drug substance is then dissolved in solution and aliquoted into small vials for individual dosing. Each of these steps involves a relatively routine chemical engineering process. We expect the costs associated with manufacturing drug product 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. Separate third-party manufacturers are for fill and finish services and for labeling and shipment of the final drug products to the clinical trial sites.

We have introduced improvements to the manufacturing process in order to eliminate impurities like those that we believe caused inflammation in our Phase 3 trials in GA and our Phase 1b/2 trial in wet AMD. We believe that the improved manufacturing process can be used to supply pegcetacoplan at a scale required for our clinical trials and global commercialization. In non-clinical testing, treatment with pegcetacoplan manufactured through the improved manufacturing process did not cause inflammation.

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, reimbursement, 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.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory

alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

On December 13, 2016, the 21st Century Cures Act established (and the 2017 Food and Drug Administration Reauthorization Act later amended) a requirement that sponsors of one or more investigational drugs for the treatment of a serious disease(s) or condition(s) make publicly available their policy for evaluating and responding to requests for expanded access for individual patients. Although these requirements were rolled out over time, they have now come into full effect. This provision requires drug and biologic companies to make publicly available their policies for expanded access for individual patient access to products intended for serious diseases. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study; or 15 days after the drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy

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.

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.

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.

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 2020 is $2,942,965 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 2020 is $325,424. 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

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.

A clinical trial is typically required for a PMA application and, in a small percentage of cases, the FDA may require a clinical study in support of a 510(k) submission. A manufacturer that wishes to conduct a clinical study involving the device is subject to the FDA's IDE regulation. The IDE regulation distinguishes between significant and non-significant risk device studies and the procedures for obtaining approval to begin the study differ accordingly. Also, some types of studies are exempt from the IDE regulations. A significant risk device presents a potential for serious risk to the health, safety, or welfare of a subject. Significant risk devices are devices that are substantially important in diagnosing, curing, mitigating, or treating disease or in preventing impairment to human health. Studies of devices that pose a significant risk require both FDA and an IRB approval prior to initiation of a clinical study. Non-significant risk devices are devices that do not pose a significant risk to the human subjects. A non-significant risk device study requires only IRB approval prior to initiation of a clinical study.

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. 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. As of January 1, 2020, the website of the European Commission reported that the implementation of the Clinical Trials Regulation was dependent on the development of a fully functional clinical trials portal and database, which would be confirmed by an independent audit, and that the new legislation would come into effect six months after the European Commission publishes a notice of this confirmation. The website indicated that the audit was expected to commence in December 2020.

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.

As in the United States, similar requirements for posting clinical trial information are present in the European Union (EudraCT) website: https://eudract.ema.europa.eu/ and other countries.

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”). Following protracted negotiations, the United Kingdom left the European Union on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable up to two years). Discussions between the United Kingdom and the European Union have so far mainly focused on finalizing withdrawal issues and transition agreements but have been extremely difficult to date. To date, only an outline of a trade agreement has been reached. Much remains open but the Prime Minister has indicated that the United Kingdom will not seek to extend the transitional period beyond the end of 2020. If no trade agreement has been reached before the end of the transitional period, there may be significant market and economic disruption. The Prime Minister has also indicated that the UK will not accept high regulatory alignment with the EU.

Since the regulatory framework for pharmaceutical products in the United Kingdom 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 that applies to products and the approval of product candidates in the United Kingdom. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation (GDPR), which became effective on May 25, 2018. The GDPR is

wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

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 ass/ure 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 Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;
- 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, and continue to be, 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, became effective in 2019. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax, and effective January 1, 2021, also eliminates the health insurer tax. Further, the Bipartisan Budget Act of 2018, among other things, amended 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 may 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. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs 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. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. This decision is under review by the U.S. Supreme Court during its current term. The full effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

In addition, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. The Trump administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. The Trump Administration recently represented to the Court of Appeals considering this judgment that it does not oppose the lower court's ruling. On July 10, 2019, the Court of Appeals for the Fifth Circuit heard oral argument in this case.

On December 18, 2019, that court affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. On January 21, 2020, the U.S. Supreme Court declined to review this decision on an expedited basis. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted 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. For example, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted 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, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the Administration issued a plan to lower drug prices. Under this blueprint for action, the Administration indicated that the Department of Health and Human Services (HHS) will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases. In addition, on December 23, 2019, the Trump Administration published a proposed rulemaking that, if finalized, would allow states or certain other non-federal government entities to submit importation program proposals to FDA for review and approval. Applicants would be required to demonstrate their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. At the same time, FDA issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

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. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Scientific Advisory Boards

Our scientific advisory board includes physicians and scientists recognized as authorities in the areas of hematology, neurology, nephrology, 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.

Employees

As of December 31, 2019, we had 235 full-time or part-time employees, including 4 employees with M.D./Ph.D. degrees, 4 employees with an M.D. degree and 22 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.

Corporate Information

We were incorporated under the laws of the State of Delaware on September 25, 2009 under the name Apellis Pharmaceuticals, Inc. Effective January 1, 2020, our principal executive office is located at 100 Fifth Avenue, Waltham, Massachusetts and our telephone number is 617-977-5700. Previously our principal executive office was located in Crestwood, Kentucky.

Available Information

We file reports and other information with the Securities and Exchange Commission as required by the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. You can review our electronically filed reports and other information that we file with the SEC on the SEC's web site at http://www.sec.gov.

Our website address is www.apellis.com. We make available free of charge through our 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. In addition, we regularly use our website to post information regarding our business, product development programs and governance, and we encourage investors to use our website, particularly the information in the section entitled "Investors & Media," as a source of information about us.

The foregoing references to our website are not intended to, nor shall they be deemed to, incorporate information on our website into this Annual Report on Form 10-K by reference.

Item 1A. Risk Factors.

Careful consideration should be given to the following risk factors, in addition to the other information set forth in this Annual Report on Form 10-K and in other documents that we file with the SEC, in evaluating our company and our business. Investing in our common stock involves a high degree of risk. If any of the following risks actually occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

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 $51.0 million, $127.5 million and $304.7 million for the years ended December 31, 2017, 2018 and 2019, respectively. As of December 31, 2019, we had an accumulated deficit of $581.5 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 subsequent follow-on offerings, the sale of convertible notes, private placements of our preferred stock, the development funding agreement with SFJ Pharmaceuticals Group, or SFJ, borrowings under a term loan facility and the issuance and sale of a promissory note. 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, pegcetacoplan;
- 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 our stockholders to lose all or part of their investment.

We have not yet successfully obtained marketing approvals nor commercialized pharmaceutical products, which may make it difficult to evaluate our future prospects.

Our operations to date have been limited to financing and staffing our company, developing our technology and conducting preclinical research and Phase 1, Phase 2 and Phase 3 clinical trials for our product candidates. However, although we have begun planning commercial activities, we have not yet demonstrated an ability to successfully 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, our stockholders should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by clinical-stage biopharmaceutical companies such as ours. Any predictions made 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, our stockholders 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, 2017, 2018 and 2019, we used net cash of $46.6 million, $131.2 million and $211.1 million respectively, in our operating activities substantially all of which related to research and development activities. As of December 31, 2019, our cash and cash equivalents were $352.0 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 incur significant 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 will be required to expend significant funds in order to advance the development of pegcetacoplan 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, our existing cash and cash equivalents will not be sufficient to complete all of our ongoing Phase 3 clinical trials of pegcetacoplan or to complete development of pegcetacoplan 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 our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements at least into mid-2021. Our estimate as to how long we expect our 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. Although we expect that our cash and cash equivalents will allow us to announce top-line data on the primary efficacy endpoint in our DERBY and OAKS trials, we would not be able to complete the 24 month observation intervals for the DERBY and OAKS clinical trials or complete the clinical and commercial development of pegcetacoplan or any of our other product candidates. 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, will depend on many factors, including:

- the scope, progress, timing, costs and results of clinical trials of, and research and preclinical development efforts for, pegcetacoplan, APL-9 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, 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, the ownership interest of our then-existing stockholders may be diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect the rights of our common stockholders. In addition, additional 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, under our development funding agreement with SFJ, as amended, we have agreed that following regulatory approval by the U.S. Food and Drug Administration, or FDA, or the European Medicines Agency, or EMA, for the use of pegcetacoplan as a treatment for paroxysmal-nocturnal hemoglobinuria, or PNH we will pay to SFJ an initial payment of up to $5.0 million (or up to a total of $10.0 million if regulatory approval is granted by the FDA and the EMA) and then up to an additional $226.0 million in the aggregate (or up to $452.0 million if regulatory approval is granted by the FDA and the EMA) in six additional annual payments with the majority of the payments being made from the third anniversary to the sixth anniversary of regulatory approval. Such payments will be proportionately adjusted in the event that the actual funding from SFJ is lower or greater than $120.0 million (including as a result of the payment of the Additional SFJ Funding but excluding the $20.0 million funding payment made under the SFJ amendment). Additionally, we granted a security interest in all of our assets, excluding our intellectual property and license agreements to which we are a party. In connection with the grant of the security interest, we agreed to certain affirmative and negative covenants, including restrictions on our ability to pay dividends, incur additional debt or enter into licensing transactions with respect to our intellectual property other than specified types of licenses.

Future debt securities or other financing arrangements could contain similar or more restrictive negative covenants. 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.

If we receive regulatory approval for the use of pegcetacoplan as a treatment for PNH or if our agreement with SFJ is terminated prior to receiving such approval in specified circumstances, we will be required to make substantial payments to SFJ pursuant to our development funding agreement. If we do not have sufficient funding or cash flow from our business to meet our payment obligations under the development funding agreement, SFJ could exercise its remedies as a holder of a first priority security interest in our assets and our business could be materially harmed.

If we receive regulatory approval for the use of pegcetacoplan as a treatment for PNH, we will be required to make substantial payments to SFJ pursuant to our development funding agreement. In addition, if the agreement is terminated prior to obtaining regulatory approval for the treatment of PNH, under specified circumstances, we also will be required to make substantial payments to SFJ. Our ability to make these required payments depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may generate cash flow from operations in the future sufficient to meet our obligations under the development funding agreement. If we are unable to generate such cash flow or to obtain additional funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources on acceptable terms or at all, we could default on our payment obligations to SFJ.

Our payment obligations to SFJ could have significant consequences for our security holders and our business, results of operations and financial condition by, among other things:

- limiting our ability to obtain additional financing;
- requiring the dedication of a substantial portion of our cash flow from operations to service our meet our obligations under the development funding agreement, which will reduce the amount of cash available for other purposes; and
- limiting our flexibility to plan for, or react to, changes in our business;

Our business may not generate sufficient funds, and we may otherwise be unable to maintain sufficient cash reserves, to pay amounts due to SFJ, and our cash needs may increase in the future.

We have granted SFJ a first priority security interest in all of our assets other than our intellectual property and the license agreements to which we are a party. If we are unable to meet our payment obligations to SFJ, SFJ may exercise its remedies as a holder of a first priority security interest, which would result in a loss of our assets and our business would be materially harmed.

Our indebtedness could limit the cash flow available for our operations, expose us to risks that could adversely affect our business, financial condition and results of operations and impair our ability to satisfy our obligations under the Convertible Notes.

We incurred $220.0 million of indebtedness as a result of the sale of the convertible notes in September 2019, or the Convertible Notes. We may also incur additional indebtedness to meet future financing needs. Our indebtedness could have significant negative consequences for our security holders and our business, results of operations and financial condition by, among other things:

- increasing our vulnerability to adverse economic and industry conditions;
- limiting our ability to obtain additional financing;
- requiring the dedication of a substantial portion of our cash flow from operations to service our indebtedness, which will reduce the amount of cash available for other purposes;
- limiting our flexibility to plan for, or react to, changes in our business;

- diluting the interests of our existing stockholders as a result of issuing shares of our common stock upon conversion of the Convertible Notes; and
- placing us at a possible competitive disadvantage with competitors that are less leveraged than us or have better access to capital.

Our business may not generate sufficient funds, and we may otherwise be unable to maintain sufficient cash reserves, to pay amounts due under the Convertible Notes, and our cash needs may increase in the future.

Servicing the Convertible Notes will require a significant amount of cash, and we may not have sufficient cash flow from our business to make payments on the Convertible Notes.

Our ability to make scheduled payments of the principal of, to pay interest on or to refinance the Convertible Notes depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may not generate cash flow from operations in the future sufficient to service the Convertible Notes. If we are unable to generate cash flow, we may be required to adopt one or more alternatives, such as selling assets, restructuring debt or obtaining additional equity capital on terms that may be unfavorable to us or highly dilutive. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at the time we seek to refinance such indebtedness. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

We may not have the ability to raise the funds necessary to settle conversions of the Convertible Notes in cash or to repurchase the Convertible Notes upon a fundamental change, and our future debt may contain limitations on our ability to pay cash upon conversion or repurchase of the Convertible Notes.

Holders of the Convertible Notes have the right to require us to repurchase all or a portion of their Convertible Notes upon the occurrence of a fundamental change at a price equal to the principal amount of the Convertible Notes to be repurchased, plus accrued and unpaid interest. In addition, upon conversion of the Convertible Notes, unless we elect to deliver solely shares of our common stock to settle such conversion (other than paying cash in lieu of delivering any fractional share), we will be required to make cash payments in respect of the Convertible Notes being converted. However, we may not have enough available cash or be able to obtain financing at the time we are required to make repurchases of Convertible Notes surrendered therefor or Convertible Notes being converted. In addition, our ability to repurchase the Convertible Notes or to pay cash upon conversions of the Convertible Notes may be limited by law, by regulatory authority or by agreements governing our future indebtedness. Our failure to repurchase Convertible Notes at a time when the repurchase is required by the indenture or to pay any cash payable on future conversions of the Convertible Notes as required by the indenture would constitute a default under the indenture. A default under the indenture or the fundamental change itself could also lead to a default under agreements governing our existing or future indebtedness. If the repayment of the related indebtedness were to be accelerated after any applicable notice or grace periods, we may not have sufficient funds to repay the indebtedness and repurchase the Convertible Notes or make cash payments upon conversions thereof.

The conditional conversion feature of the Convertible Notes, if triggered, may adversely affect our financial condition and operating results.

In the event the conditional conversion feature of the Convertible Notes is triggered, holders of Convertible Notes will be entitled to convert the Convertible Notes at any time during specified periods at their option. If one or more holders elect to convert their Convertible Notes, unless we elect to satisfy our conversion obligation by delivering solely shares of our common stock (other than paying cash in lieu of delivering any fractional share), we would be required to settle a portion or all of our conversion obligation in cash, which could adversely affect our liquidity. In addition, even if holders do not elect to convert their Convertible Notes, we could be required under applicable accounting rules to reclassify all or a portion of the outstanding principal amount of the Convertible Notes as a current rather than long-term liability, which would result in a material reduction of our net working capital.

The accounting method for convertible debt securities could have a material effect on our reported financial results.

In May 2008, the Financial Accounting Standards Board, or FASB, issued FASB Staff Position No. APB 14-1, Accounting for Convertible Debt Instruments That May Be Settled in Cash Upon Conversion (Including Partial Cash Settlement), which has subsequently been codified as Accounting Standards Codification 470-20, Debt with Conversion and Other Options, or ASC 470-20. Under ASC 470-20, an entity must separately account for the liability and equity components of the convertible debt instruments (such as the Convertible Notes) that may be settled entirely or partially in cash upon conversion in a manner that reflects the issuer’s economic interest cost. The effect of ASC 470-20 on the accounting for the Convertible Notes is that the equity component is required to be included in the additional paid-in capital section of stockholders’ equity on our consolidated balance sheet, and the value of the equity component would be treated as original issue discount for purposes of accounting for the debt component of the Convertible Notes. As a result, we will be required to record a greater amount of non-cash interest expense in current periods presented as a result of the amortization of the discounted carrying value of the Convertible Notes to their face amount over the term of the Convertible Notes. We will report lower net income in our financial results because ASC 470-20 will require interest to include both the current

period's amortization of the debt discount and the instrument's coupon interest, which could adversely affect our reported or future financial results, the trading price of our common stock and the trading price of the Convertible Notes.

In addition, under certain circumstances, convertible debt instruments (such as the Convertible Notes) that may be settled entirely or partly in cash are currently accounted for utilizing the treasury stock method, the effect of which is that the shares issuable upon conversion of the Convertible Notes are not included in the calculation of diluted earnings per share except to the extent that the conversion value of the Convertible Notes exceeds their principal amount. Under the treasury stock method, for diluted earnings per share purposes, the transaction is accounted for as if the number of shares of common stock that would be necessary to settle such excess, if we elected to settle such excess in shares, are issued. We cannot be sure that the accounting standards in the future will continue to permit the use of the treasury stock method. If we are unable to use the treasury stock method in accounting for the shares issuable upon conversion of the Convertible Notes, then our diluted earnings per share would be adversely affected.

In July 2019, the FASB issued an exposure draft that proposes to change the accounting for the convertible debt instruments described above. Under the exposure draft, an entity may no longer be required to separately account for the liability and equity components of convertible debt instruments. This could have the impact of reducing non-cash interest expense, and thereby increasing net income. Additionally, as currently proposed, the treasury stock method for calculating earnings per share will no longer be allowed for convertible debt instruments whose principal amount may be settled using shares. Rather, the if-converted method may be required, which would decrease our diluted weighted-average earnings per share. We cannot be sure that this exposure draft will be issued, or will be issued in its current format. We also cannot be sure whether other changes may be made to the current accounting standards related to the Convertible Notes, or otherwise, that could have an adverse impact on our financial statements.

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 pegcetacoplan or other product candidates.

Pegcetacoplan is a novel therapeutic compound and its potential benefit in controlling autoimmune and inflammatory diseases has not been established. Pegcetacoplan 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, pegcetacoplan 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 pegcetacoplan or any other product candidates in a pivotal trial or obtained marketing approval of any product candidate. We have evaluated pegcetacoplan in preclinical studies and in clinical trials, and have advanced pegcetacoplan into Phase 3 clinical development in geographic atrophy, or GA, PNH, but 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 pegcetacoplan 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, pegcetacoplan***. 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 pegcetacoplan. Our prospects are substantially dependent on our ability, or that of any future collaborator, to develop, obtain marketing approval for and successfully commercialize pegcetacoplan in one or more disease indications.

The success of pegcetacoplan will depend on several factors, including the following:

- successful recruitment of patients, enrollment in and completion of our ongoing and planned clinical trials;
- initiation and successful recruitment of patients, enrollment in and completion of additional clinical trials;
- safety, tolerability and efficacy profiles that are satisfactory to the FDA, EMA or any comparable foreign regulatory authority for marketing approval;
- our ability to identify success criteria and endpoints for our clinical trials and otherwise design our clinical trials such that the FDA, 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 extent of any required post-marketing approval commitments to applicable regulatory authorities;

- establishment of supply arrangements with third-party suppliers and manufacturers of raw materials and drug intermediates;
- 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;
- the performance of our future collaborators, if any;
- obtaining pegcetacoplan drug product from third-party manufacturers of sufficient quality to be used in our clinical trials and for commercial sale;
- 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 pegcetacoplan 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.

In October 2018, we announced that we voluntarily implemented a pause in dosing in our Phase 3 clinical program in patients with GA due to observed cases of non-infectious inflammation in patients treated from a single manufacturing lot of pegcetacoplan

intravitreal drug product. We also voluntarily implemented a pause in our Phase 1b/2 trial of pegcetacoplan in patients with wet AMD, which we subsequently discontinued. A total of eight patients, four in the Phase 3 GA program and four in our Phase 1b/2 clinical trial of pegcetacoplan in patients with wet AMD, were treated with pegcetacoplan from this manufacturing lot and each patient developed non-infectious inflammation. Inflammation in all eight patients completely resolved. We reviewed these events with the data safety monitoring board for the ophthalmology program, conducted a series of non-human studies and introduced improvements to the manufacturing process. Based on these efforts, we believe that the likely source of inflammation resided in an impurity in the active pharmaceutical ingredient that was introduced by the scale-up of the manufacturing process to produce commercial lot sizes. We modified our manufacturing process in order to eliminate the impurity and have manufactured sufficient supply of pegcetacoplan utilizing the modified manufacturing process to conduct the Phase 3 GA program. In March 2019, we restarted enrollment of our Phase 3 clinical program in GA.

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 pegcetacoplan 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.

In addition, in preclinical studies of pegcetacoplan, we observed evidence of minimal to mild kidney toxicity when animals were administered relatively higher doses of pegcetacoplan 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 pegcetacoplan. If such kidney toxicity, or other adverse effects, were to arise in patients being treated with pegcetacoplan 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 pegcetacoplan 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 pegcetacoplan, 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 pegcetacoplan every month and 9% of patients who received administration of pegcetacoplan every other month showed new onset exudation in the study eye as compared to 1% of the sham group. As we continue development of pegcetacoplan for GA, if a significant number of patients develop new onset exudation, then we may need to limit development of intravitreal pegcetacoplan 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.

In our Phase 3 clinical trial of pegcetacoplan in patients with GA and our Phase 1b/2 clinical trial of pegcetacoplan in patients with wet AMD, several patients treated from a single manufacturing lot of pegcetacoplan intravitreal drug product experienced non-infectious inflammation. A total of eight patients, four in our Phase 3 GA program and four in our Phase 1b/2 clinical trial of pegcetacoplan in patients with wet AMD, were treated with this pegcetacoplan from this manufacturing lot and each patient developed non-infectious inflammation. Inflammation in these patients has completely resolved.

In our Phase 3 PEGASUS trial, the most common adverse events reported during the 16-week, randomized, controlled treatment period in the pegcetacoplan and eculizumab groups, respectively, were injection site reactions (36.6% vs. 2.6%), diarrhea (22.0% vs. 0%), headache (7.3% vs. 20.5%) and fatigue (4.9% vs. 15.4%). Another common adverse event was hemolysis, which was reported in four patients in the pegcetacoplan group (9.8%) and nine patients in the eculizumab group (23.1%) and which led to three discontinuations in pegcetacoplan group.

In our Phase 1b trial of pegcetacoplan in patients receiving treatment with eculizumab, one serious adverse event was noted as possibly related to the administration of pegcetacoplan. The patient with this serious adverse event experienced liver pain and elevated liver enzyme levels. As a result, treatment with pegcetacoplan 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 pegcetacoplan 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 pegcetacoplan in treatment-naïve patients, we learned that one patient with concomitant aplastic anemia developed bone marrow failure after one year of treatment with pegcetacoplan. Treatment with pegcetacoplan was discontinued on November 14, 2017. The investigator determined that the bone marrow failure in this patient was not related to the administration of pegcetacoplan. 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 pegcetacoplan could not have contributed to the bone marrow failure experienced by this patient.

In addition, in our Phase 1b clinical trial of pegcetacoplan treatment naïve patients with PNH, one patient, who had been temporarily discontinued from dosing with pegcetacoplan due to an unrelated medical condition, experienced increased hemolysis and required a transfusion. This was classified as a serious adverse event unrelated to the administration of pegcetacoplan. This patient subsequently recovered and has resumed treatment with pegcetacoplan. We believe that a sudden discontinuation of pegcetacoplan may cause increased hemolysis in some patients. Another patient in this study had a hypersensitivity reaction which resolved without further complications, which was classified as a serious adverse event possibly related to the administration of pegcetacoplan.

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;
- 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, including the data from our PEGASUS trial;
- 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, drug intermediates or manufactured product candidates, other products evaluated in our clinical trials 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 pegcetacoplan for the treatment of PNH is dependent upon our ability to enroll a sufficient number of patients with PNH. PNH, cold agglutinin disease, or CAD, and C3 glomerulopathy, or C3G are rare diseases with a small patient population, and many of those patients are treated with other therapies or products. Further, there are only a limited number of specialist physicians that regularly treat patients with these rare diseases and major clinical centers that support such 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 these rare diseases 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 these indications and the expectation that many patients will be on treatment with other therapies or products, we may encounter difficulty in recruiting a sufficient number of patients for our trials including in particular our planned clinical 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 pegcetacoplan 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 pegcetacoplan 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 pegcetacoplan, *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 are similar in design to the Phase 2 clinical trial, except that patients will be treated with pegcetacoplan for 24 months rather than 12 months and there will not be a six-month monitoring period following treatment. Additionally, unlike the Phase 2 clinical trial, GA lesion size will be measured by total area rather than mean change in the square root of GA lesion size. In our Phase 3 clinical trials in GA, statistical significance is set 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 clinical trial, 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 pegcetacoplan 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 pegcetacoplan, 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.

We intend to meet with regulatory agencies in the first half of 2020 to discuss what information is required to support regulatory submissions of an NDA and an MAA for pegcetacoplan in PNH. The FDA has advised us that, for the approval of a new treatment for PNH, hemoglobin stabilization in conjunction with change in transfusion dependence constitute accepted clinical benefit, but that a rise in hemoglobin levels may not translate to clinical benefit in patients who entered the trial with high hemoglobin levels, such as permitted by the inclusion criteria of the PEGASUS trial, and who do not require transfusions. We believe that the data from the PEGASUS trial support a finding of clinical benefit. As clinical data is susceptible to varying interpretations and analyses, we will need to discuss our data with the FDA, European Medicines Agency, or EMA, and other regulatory agencies before we can determine our next steps.

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 (marketed as Soliris) and ravulizumab (marketed as Ultomiris) are the only therapies that have been approved for the treatment of PNH, and even if we are able to obtain marketing approval of pegcetacoplan for the treatment of PNH, we may not be able to successfully convince physicians or patients to switch from eculizumab or ravulizumab to pegcetacoplan. 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 are currently developing sales, marketing and distribution infrastructure to support commercialization of our product candidates.

We are building 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 requires substantial resources, is 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 by Novartis AG as a monotherapy or adjunctive therapy with LFG316, an anti-C5 monoclonal antibody, in Phase 2 clinical trials; Zimura, a C5 inhibitor being developed by Iveric bio (formerly known as Ophthotech Corporation) 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 therapies being developed by Alcon, Allegro Ophthalmics LLC, Allergan PLC, Cell Cure Neurosciences, Genentech, Hemera Biosciences, Ionis Pharmaceuticals, Inc., Janssen Research & Development, LLC, Regenerative Patch Technologies, Stealth, Gyroscope Therapeutics, and BioTime, Inc. In October 2019 Alexion obtained an option to co-develop and commercialize elamipretide for certain indications, including GA, from Stealth. Stealth is evaluating elamipretide in a Phase 2 clinical trial in patients with GA.

The principal competitors for PNH, and possibly other indications in our hematology and nephrology programs are eculizumab (marketed as Soliris) and ravulizumab (marketed as Ultomiris), C5 inhibitors developed and marketed by Alexion. Eculizumab and ravulizumab are the only drugs currently approved for the treatment of PNH.

We are aware of several other companies that are actively developing product candidates for the treatment of PNH, including AMY-101, C3 complement inhibitor being developed by Amyndas Pharmaceuticals SA; cemdisiran, an RNAi therapeutic targeting C5 developed by Alnylam Pharmaceuticals, Inc. in early clinical trials; nomacopan, a small protein C5 complement inhibitor being developed by Akari Therapeutics, Plc. in Phase 2 clinical trials; BCX9930, a Factor D inhibitor being developed by BioCryst, currently in early clinical development; zilucoplan, a cyclic peptide C5 inhibitor developed by Ra Pharmaceuticals, Inc., or Ra, currently in Phase 2 clinical trials, crovalimab, an anti-C5 antibody developed by Roche/Chugai, currently in Phase 2 clinical trials; pozelimab, an anti-C5 antibody developed by Regeneron, currently in Phase 2 clinical trials; and LNP-023, a Factor B inhibitor being developed by Novartis currently in Phase 2 clinical trials; 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. Alexion is developing danicopan, formerly ACHN-4471, an orally available complement factor D inhibitor, currently in Phase 2 clinical trials as a cotreatment or combination product with eculizumab, and next generation complement factor D inhibitors ACHN-5528 and ACHN-5548 in early clinical development. Amgen is developing ABP959, a biosimilar for eculizumab that is in Phase 3 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 CAD but treatments in development, include sutimlimab, a C1s monoclonal antibody inhibitor, being developed by Sanofi, in Phase 3 clinical trials; parsaclisib, a PI3K-d inhibitor, being developed by Incyte, in Phase 2 clinical trials; and KZR-616, a proteasome inhibitor, being developed by Kezar Lifesciences, in Phase 2 clinical trials.

There are no currently marketed drug treatments for C3 glomerulopathy, but treatments in development include narsoplimab (OMS721), a human monoclonal antibody to mannose-binding lectin-associated serine protease-2 (MASP-2) that blocks the lectin pathway, being developed by Omeros Corp., in Phase 2 clinical trials; avacopan, an oral C5aR-inhibitor developed by ChemoCentryx, Inc., in Phase 2 clinical trials; LNP023, a complement factor inhibitor being developed by Novartis, for C3 glomerulopathy is in Phase 2 clinical trials; and danicopan, being developed by Alexion for C3G, in Phase 2 clinical trials.

In October 2019, the acquisition of Ra by UCB S.A. was announced. Ra and UCB S.A. have stated that they expect the acquisition to close in the first quarter of 2020, pending satisfaction of closing conditions and approval from relevant regulatory agencies.

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.

Our internal information systems, or those of any contractors, consultants, vendors, business partners or other third parties, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

We collect, store and transmit large amounts of confidential information, including personal information and information relating to intellectual property, on internal information systems and through the information systems of our contractors, consultants, vendors, business partners or other third parties.

Despite the implementation of security measures, our internal information systems and those of third parties are vulnerable to damage from computer viruses, malware, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such systems are also vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, our collaborators, contractors, consultants, vendors, business partners and other third parties, or from cyber-attacks by malicious third parties over the Internet or through other mechanisms. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, ransomware, denial of service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyber-attacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient.

While we have not experienced any such material system failure, accident, cyber-attack or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs, clinical trials and business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from clinical trials could result in delays or termination of our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, as risks with respect to our information systems continue to evolve, we will incur additional costs to maintain the security of our information systems and comply with evolving laws and regulations pertaining to cybersecurity and related areas. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, including regulatory fines and other losses with respect to privacy claims, enrollment in our clinical trials could be negatively affected, our competitive position and reputation could be harmed and the further development and commercialization of our product candidates could be delayed.

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 pegcetacoplan 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 experienced issues associated with the manufacturing process for pegcetacoplan that resulted in delays in the supply of pegcetacoplan. These delays resulted in us incurring additional costs and delays in our PNH development program. Additionally, in October 2018, we announced that we voluntarily implemented a pause in dosing in our Phase 3 clinical program in patients with GA due to observed cases of non-infectious inflammation in patients treated from a single manufacturing lot of pegcetacoplan intravitreal drug product that we believe occurred due to an impurity in the active pharmaceutical ingredient. If we experience other issues or delays in the future, our development of pegcetacoplan 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 pegcetacoplan. 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 pegcetacoplan. 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 may not be able to meet our supply requirements for clinical and commercial operations and 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 pegcetacoplan through subcutaneous infusion. While this device is in development, we plan to 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 candidates, pegcetacoplan and APL-9, and that specifically recite the active component. 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 pegcetacoplan. Although we believe that these claims, if construed to cover pegcetacoplan, 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 January 31, 2020 the United Kingdom formally withdrew from the European Union. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable up to two years). Discussions between the United Kingdom and the European Union have so far mainly focused on finalizing withdrawal issues and transition agreements but have been extremely difficult to date. To date, only an outline of a trade agreement has been reached. Much remains open but the Prime Minister has indicated that the United Kingdom will not seek to extend the transitional period beyond the end of 2020. If no trade agreement has been reached before the end of the transitional period, there may be significant market and economic disruption. The Prime Minister has also indicated that the UK will not accept high regulatory alignment with the EU.

Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, Brexit 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 significantly and materially 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 may 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 pegcetacoplan for the treatment of PNH and for the treatment of C3 glomerulopathy. 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 pegcetacoplan 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.

We have received fast track designations for pegcetacoplan for the treatment of PNH and GA. 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 pegcetacoplan for the treatment of PNH and GA, 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% 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 2029 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.

Since enactment of the ACA, there have been, and continue to be, 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. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. Further, the Bipartisan Budget Act of 2018, among other things, amended 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 may 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. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs 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. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. This decision is under review by the U.S. Supreme Court during its current term. The full effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

In addition, the Centers for Medicare & Medicaid Services, or CMS, has proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. On November 30, 2018, CMS announced a proposed rule that would amend the Medicare Advantage and Medicare Part D prescription drug benefit regulations to reduce out of pocket costs for plan enrollees and allow Medicare plans to negotiate lower rates for certain drugs. Among other things, the proposed rule changes would allow Medicare Advantage plans to use pre authorization (PA) and step therapy (ST) for six protected classes of drugs, with certain exceptions, permit plans to implement PA and ST in Medicare Part B drugs; and change the definition of "negotiated prices" while a definition of "price concession" in the regulations. It is unclear whether these proposed changes we be accepted, and if so, what effect such changes will have on our business. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. The Trump administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. The Trump Administration recently represented to the Court of Appeals considering this judgment that it does not oppose the lower court's ruling. On July 10, 2019, the Court of Appeals for the Fifth Circuit heard oral argument in this case. On December 18, 2019, that court affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. On January 21, 2020, the U.S. Supreme Court declined to review this decision on an expedited basis. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

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 annual 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.

Specifically, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted 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, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the Administration issued a plan to lower drug prices. Under this blueprint for action, the Administration indicated that the Department of Health and Human Services (HHS) will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases. In addition, on December 23, 2019, the Trump Administration published a proposed rulemaking that, if finalized, would allow states or certain other non-federal government entities to submit importation program proposals to FDA for review and approval. Applicants would be required to demonstrate their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. At the same time, FDA issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

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. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

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.

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

We continue to 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. During 2019, the number of our employees increased from 80 on December 31, 2018 to 235 on December 31, 2019 and we expect the number of employees to increase significantly in 2020. Our principal office is located in Massachusetts and we maintain additional offices in Kentucky, California and Switzerland. 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

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 the ability of stockholders to sell their shares. 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.

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

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. 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, our stockholders may not be able to sell their common stock at or above the price they paid for their common stock. The market price for our common stock may be influenced by many factors, including:

- the timing and results of clinical trials of pegcetacoplan and any other product candidates;

- the success of existing or new competitive products or technologies;
- results of discussions with regulatory authorities and 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;
- 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;
- short positions, hedging or other transactions in our securities in connection with our Convertible Notes;
- 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 our funds and may not use them effectively.

Our management will have broad discretion in the application of our cash and cash equivalents and could spend our funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could 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 our funds in a manner that does not produce income or that loses value.

We 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 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, especially as we are no longer an "emerging growth company", as defined in the Jumpstart Our Business Startups Act of 2012, and are no longer able to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are "emerging growth companies" and were applicable to us prior to January 1, 2019.

Pursuant to SOX Section 404, we are required to furnish with our periodic Exchange Act reports a report by our management on our internal control over financial reporting and we are required to include with our annual report on Form 10-K 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 have been engaged in a process to document and evaluate our internal control over financial reporting, which has been, and will continued to be, both costly and challenging. In this regard, we will need to continue to dedicate internal resources, 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, from time to time, 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.

If we identify a material weakness in our internal control over financial reporting, it could have an adverse effect on our business and financial results and our ability to meet our reporting obligations could be negatively affected, each of which could negatively affect the trading price of our common stock.

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. Accordingly, a material weakness increases the risk that the financial information we report contains material errors.

We regularly review and update our internal controls, disclosure controls and procedures, and corporate governance policies. In addition, we are required under the Sarbanes-Oxley Act of 2002 to report annually on our internal control over financial reporting. Our system of internal controls, however well-designed and operated, is based in part on certain assumptions and includes elements that rely on information from third parties. Our system can provide only reasonable, not absolute, assurances that the objectives of the system are met. If we, or our independent registered public accounting firm, determine that our internal controls over financial reporting are not effective, or we discover areas that need improvement in the future, these shortcomings could have an adverse effect on our business and financial results, and the price of our common stock could be negatively affected.

If we cannot conclude that we have effective internal control over our financial reporting, or if our independent registered public accounting firm is unable to provide an unqualified opinion regarding the effectiveness of our internal control over financial reporting, investors could lose confidence in the reliability of our financial statements, which could lead to a decline in our stock price. Failure to comply with reporting requirements could also subject us to sanctions and/or investigations by the SEC, The Nasdaq Stock Market or other regulatory authorities.

A sale of a substantial number of shares of our common stock 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. As of February 21, 2020, we had 75,321,471 shares of common stock outstanding. All of these shares 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 and subject to the volume limitations applicable to affiliates.

We intend to register all shares of common stock that we may issue under our equity compensation plans. As of December 31, 2019, we had options to purchase an aggregate of 10,854,437 shares of our common stock outstanding, of which options to purchase 4,808,730 shares were vested. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates. Moreover, holders of an aggregate of 11,153,094 shares of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements 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 Tax Cuts and Jobs Act could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law new legislation, commonly referred to as the Tax Cuts and Jobs Act, or the TCJA, that significantly revised the Internal Revenue Code of 1986, as amended. The TCJA, 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 federal tax law remains uncertain and our business and financial condition could be adversely affected. In addition, how various states will respond to the TCJA continues to be uncertain. 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, 2019, we had both federal and state net operating loss carryforwards of $392.9 million and $358.3 million, respectively, and federal research and development tax credit carryforwards of $24.2 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 development funding agreement with SFJ, 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 our stockholders’ 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 21, 2020, our executive officers and directors, and entities associated or affiliated with our executive officers and directors, in the aggregate, beneficially owned shares representing approximately 25.5% of our outstanding common stock, including our largest stockholder, Morningside Venture Investments, Ltd., which beneficially owned approximately 16.7% of our outstanding common stock. 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 those of our other investors. For example, because many of these stockholders purchased their shares at prices substantially below the price at which other investors purchased shares 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 our stockholders might otherwise receive a premium for their 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 the best interests of our stockholders. 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 certificate of incorporation or 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.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our facilities consist of office space of approximately 61,417 square feet in Waltham, Massachusetts under a lease that expires in June 2025, office space of approximately 9,478 square feet in San Francisco, California under a lease that expires in April 2024; office space of 7,125 square feet in Crestwood, Kentucky under a lease that expires in July 2023, and temporary office space in Zug, Switzerland.

Item 3. Legal Proceedings.

We are not currently subject to any material legal proceedings.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock has been listed on the Nasdaq Global Select Market under the symbol "APLS" since November 9, 2017. Prior to that date, there was no public trading market for our common stock.

Holders of Record

As of February 21, 2020, we had 24 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 or paid cash dividends on our capital stock. In addition, our development agreement with SFJ 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 intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors.

Securities Authorized for Issuance under Equity Compensation Plans

Information about our equity compensation plans is incorporated by reference herein to Item 12 of Part III of this Annual Report on Form 10-K.

Stock Performance Graph

The following performance graph shall not be deemed "soliciting material" or to be "filed" with the SEC for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our future filings under the Securities Act of 1933, as amended, or the Securities Act, or the Exchange Act, except to the extent that we specifically incorporate it by reference into such filing.

The graph below compares the cumulative total stockholder return on our common stock between November 9, 2017 (the first date that shares of our common stock were publicly traded) and December 31, 2019, with the cumulative total return of (a) the Nasdaq Composite Index and (b) the Nasdaq Biotechnology Index over the same period. The graph assumes the investment of $100 after the market close on November 9, 2017 in our common stock and each of the other indices described above. The comparisons are not intended to forecast or be indicative of future performance of our common stock. All amounts shown are based on the closing price of our common stock with the exception of November 9, 2017, which is the opening price based on initial trading of our common stock. Data for the Nasdaq Composite Index and Nasdaq Biotechnology Index assume reinvestment of dividends.


Apellis Pharmaceuticals, Inc
APLS-USQ
11/09/2019 to 12/31/2019 (Daily)
250
200
150
100
50
0
11/9/2017
12/9/2017
1/9/2018
2/9/2018
3/9/2018
4/9/2018
5/9/2018
6/9/2018
7/9/2018
8/9/2018
9/9/2018
10/9/2018
11/9/2018
12/9/2018
1/9/2019
2/9/2019
3/9/2019
4/9/2019
5/9/2019
6/9/2019
7/9/2019
8/9/2019
9/9/2019
10/9/2019
11/9/2019
12/9/2019
APLS
NASDAQ Composite Index
NASDAQ Biotechnology Index

Item 6. Selected Financial Data.

The selected consolidated financial data included in this section are not intended to replace the consolidated financial statements included elsewhere in this Annual Report on Form 10-K. We derived the selected consolidated statements of operations data for the years ended December 31, 2017, 2018 and 2019 and the selected consolidated balance sheet data at December 31, 2018 and 2019 from our audited consolidated financial statements included elsewhere in this report. We have derived the consolidated statements of operations data for the years ended December 31, 2015 and 2016 and the consolidated balance sheet data as of December 31, 2015, 2016 and 2017 from our audited financial statements not included in this Annual Report on Form 10-K. Our historical results are not necessarily indicative of the results that may be expected in the future. You should read the selected historical consolidated financial data below in conjunction with the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the audited consolidated financial statements and the related notes included elsewhere in this report.

	Year Ended December 31,				
	2015	2016	2017	2018	2019
Consolidated Statements of Operations Data:					
Operating expenses:					
Research and development (1)	$ 13,730,311	$ 22,978,599	$ 40,303,878	$ 105,285,576	$ 220,968,770
Cost of acquired in-process research and development	26,486,000	—	—	—	—
General and administrative (1)	6,356,782	4,303,743	10,463,151	22,639,184	67,046,483
Operating loss	(46,573,093)	(27,282,342)	(50,767,029)	(127,924,760)	(288,015,253)
Loss on extinguishment of debt	—	—	—	—	(1,501,215)
Loss from remeasurement of development derivative liability	—	—	—	—	(14,839,000)
Interest expense (2)	—	—	(374,749)	(2,512,956)	(5,284,610)
Interest income	50,853	135,309	277,834	2,960,771	5,108,779
Other income (expense), net	6,284	22,396	(142,150)	(25,249)	(175,314)
Net loss	(46,515,956)	(27,124,637)	(51,006,094)	(127,502,194)	(304,706,613)
Net loss per common share, basic and diluted (3)	$ (8.03)	$ (3.22)	$ (3.68)	$ (2.34)	$ (4.90)
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	54,396,483	62,228,601

(1) Includes share-based compensation as follows:

	Year Ended December 31,				
	2015	2016	2017	2018	2019
Research and development	$ 171,388	$ 377,776	$ 2,678,956	$ 3,559,047	$ 10,682,553
General and administrative	374,313	701,212	2,739,754	4,174,209	10,461,476
Total share-based compensation expense	$ 545,701	$ 1,078,988	$ 5,418,710	$ 7,733,256	$ 21,144,029

(2) Includes amortization of debt discount associated with term loan facility, promissory note due to the issuance of warrants and convertible senior notes. See Note 7 to our audited consolidated financial statements included elsewhere in this report.

(3) See Note 15 in the notes to our audited consolidated financial statements appearing at the end of this document for a description of the method used to calculate basic and diluted net loss per common share.

	December 31,				
	2015	2016	2017	2018	2019
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$ 36,003,546	$ 24,863,488	$ 175,643,529	$ 176,267,666	$ 351,985,085
Working capital	34,843,678	23,729,792	175,461,348	185,414,614	307,341,865
Total assets	38,177,109	27,433,258	182,131,456	203,533,559	389,244,980
Term loan facility	—	—	19,806,944	20,388,988	—
Promissory note	—	—	6,583,402	6,655,193	—
Convertible Senior Notes	—	—	—	—	142,566,851
Development derivative liability	—	—	—	—	134,839,000
Total liabilities	3,200,160	3,638,938	33,188,596	42,560,904	355,015,304
Convertible preferred stock	77,191,906	92,054,926	—	—	—
Accumulated deficit	(71,132,922)	(98,257,559)	(149,263,653)	(276,765,847)	(581,472,460)
Total stockholders' equity	34,976,949	23,794,320	148,942,860	160,972,655	34,229,676

Item 7. 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 our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This discussion and other parts of this Annual Report on Form 10-K 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 Annual Report on Form 10-K, 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 with Phase 3 clinical trials of our lead product candidate, pegcetacoplan, in multiple indications. We believe that pegcetacoplan 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. Pegcetacoplan has already shown activity that we believe is clinically meaningful in clinical trials for several distinct medical conditions, including geographic atrophy in age-related macular degeneration, or GA; paroxysmal nocturnal hemoglobinuria, or PNH; cold agglutinin disease, or CAD; and C3 glomerulopathy, or C3G.

GA. We initiated a Phase 3 clinical program consisting of two Phase 3 clinical trials evaluating pegcetacoplan in patients with GA in September 2018. We expect that both trials will be fully enrolled by the end of the first half of 2020 and that we will announce data from these trials in mid-2021. In our Phase 2 clinical trial of pegcetacoplan in patients with GA, treatment with pegcetacoplan resulted in a significant reduction in the rate of GA lesion growth over 12 months.

PNH. In June 2018, we initiated a Phase 3 clinical trial evaluating pegcetacoplan in 80 patients with PNH who exhibited signs of moderate to severe anemia (specifically with an inclusion criterion of hemoglobin level of less than 10.5 g/dL) while being treated with eculizumab, an approved therapy for PNH that is marketed as Soliris. We refer to this trial as the PEGASUS trial.

In January 2020, we announced top-line data from the PEGASUS trial that showed that pegcetacoplan met the trial's primary efficacy endpoint, demonstrating superiority to eculizumab with a statistically significant improvement in adjusted means of 3.8 g/dL of hemoglobin at week 16 ($p < 0.0001$). At week 16, pegcetacoplan-treated patients ($n = 41$) had an adjusted mean hemoglobin increase of 2.4 g/dL from a baseline of 8.7 g/dL, compared to eculizumab-treated patients ($n = 39$) who had a change of -1.5 g/dL from a baseline of 8.7 g/dL. Additionally, pegcetacoplan showed promising results in key secondary endpoints. Pegcetacoplan met non-inferiority on transfusion avoidance and absolute reticulocyte count. Pegcetacoplan did not meet pre-specified criteria for non-inferiority on mean lactate dehydrogenase, or LDH, levels. Pegcetacoplan showed positive trends on LDH and fatigue as measured by the Functional Assessment of Chronic Illness Therapy, or FACIT, fatigue score. In the trial, the safety profile of pegcetacoplan was comparable to eculizumab.

In September 2019, we initiated a second Phase 3 clinical trial in patients with PNH who have not been treated with eculizumab, or eculizumab treatment-naïve patients. We expect to complete enrollment in this trial in the first half of 2020 and to present top-line data in the first quarter of 2021. We refer to this trial as the PRINCE trial.

We intend to meet with regulatory agencies in the first half of 2020 to discuss what information is required to support regulatory submissions of a new drug application, or NDA, or marketing authorization application, or MAA, for pegcetacoplan in PNH.

CAD. In our ongoing Phase 2 clinical trials of pegcetacoplan in patients with CAD, patients have achieved increased hemoglobin levels, reduced reticulocytes and bilirubin levels, and reduced LDH levels. We intend to disclose our plans and timing for further clinical development of pegcetacoplan for patients with CAD in the first half of 2020.

C3G. We are also conducting a Phase 2 clinical trial of pegcetacoplan for glomerular diseases with complement involvement, including C3G. We presented preliminary data on patients with C3G from this trial at the Annual Meeting of American Society of Nephropathy in November 2019. We intend to disclose our plans and timing for further clinical development of pegcetacoplan for patients with C3G in the first half of 2020.

Intravenous C3 Inhibition. We are developing compounds targeting C3 for intravenous administration. In particular, we are developing APL-9 for the prevention of complement immune system activation coincident with adeno-associated virus, or AAV, vector administration for gene therapies and other indications. APL-9 is a second generation C3 modulator and is designed to be intravenously administered for acute use.

We hold worldwide commercialization rights to pegcetacoplan, APL-9 and those 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 pegcetacoplan, building our intellectual property portfolio, organizing and staffing our company, business planning, raising capital, preparing for the commercial launch of our products 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 option to purchase additional shares of common stock, 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.

On April 23, 2018, we issued and sold 5,500,000 shares of our common stock in a follow-on public offering at a public offering price of $25.50 per share for net proceeds of $131.2 million, after deducting underwriting discounts and commissions of $8.4 million and offering expenses of $0.5 million.

On February 28, 2019, we entered into a development funding agreement, which we refer to as the SFJ agreement, with SFJ Pharmaceuticals Group or SFJ, under which SFJ agreed to provide funding to us to support the development of pegcetacoplan for the treatment of patients with PNH. Pursuant to the agreement, SFJ paid us $60.0 million following the signing of the agreement, and agreed to pay us up to an additional $60.0 million in the aggregate in three equal installments upon the achievement of specified development milestones with respect to our Phase 3 program for pegcetacoplan in PNH and subject to our having cash resources at the time sufficient to fund at least 10 months of our operations. In addition, upon the mutual agreement of us and SFJ, at any time after the earlier of the date that we have reviewed the primary endpoint data from our PEGASUS Phase 3 trial of pegcetacoplan in patients with PNH and March 31, 2020, SFJ may fund an additional $50.0 million of our development costs which we refer to as the Additional SFJ Funding.

On March 11, 2019, we issued and sold 6,900,000 shares of our common stock in a follow-on offering at a public offering price of $17.00 per share for net proceeds of $109.6 million, after deducting underwriting discounts and commissions of $7.0 million and estimated offering expenses of $0.7 million.

On June 7, 2019, we executed an amendment to the SFJ agreement, which we refer to as the SFJ amendment. Under the SFJ amendment, SFJ agreed to make an additional $20.0 million funding payment to us to support the development of pegcetacoplan for the treatment of patients with PNH. This additional $20.0 million is in addition to and not part of the Additional SFJ Funding.

On June 27, 2019, we received $40.0 million from SFJ, consisting of $20.0 million as the first installment of the additional $60.0 million upon the achievement of a milestone and the $20.0 million payable under the SFJ amendment.

On September 16, 2019, we issued and sold $220.0 million aggregate principal amount of 3.5% convertible senior notes due 2026, or Convertible Notes, in a private offering. The net proceeds from the sale of the notes were approximately $212.9 million after deducting the initial purchasers' discounts and commissions and estimated offering expenses payable. We used $28.4 million of the net proceeds from the offering to pay the cost of the capped call transactions described below. The Convertible Notes are convertible into shares of our common stock at an initial conversion rate of 25.3405 shares per $1,000 principal amount of notes (equivalent to an initial conversion price of approximately $39.46 per share of common stock). The conversion rate is subject to customary anti-dilution adjustments. In addition, following certain events that occur prior to the maturity date or if we deliver a notice of redemption, we will increase the conversion rate for a holder who elects to convert its Convertible Notes in connection with such corporate event or a notice of redemption, as the case may be, in certain circumstances as provided in the applicable indenture, or the Indenture.

In September 2019, we received $20.0 million from SFJ, as the second installment of the additional $60.0 million due to the achievement of a milestone. We met the remaining development milestones under the SFJ agreement upon the announcement of the results of the PEGASUS phase 3 trial in January 2020. The remaining $20.0 million of the additional $60.0 million installment was paid in January 2020.

On January 13, 2020, we issued and sold 10,925,000 shares of our common stock at a price per share to the public of $37.00 in a follow-on public offering including 1,425,000 shares of shares sold pursuant to the underwriters' exercise in full of their option to purchase additional shares. We received total net proceeds of $381.4 million from the sale of shares in the offering after deducting underwriting discounts and commissions of $22.2 million and estimated offering costs of approximately $0.6 million for these transactions.

To date, we have financed our operations primarily through $150.0 million in net proceeds from our IPO, $212.9 million in net proceeds from the private offering of Convertible Notes, $622.2 million in net proceeds from follow-on offerings of our common stock which includes the $381.4 million from the offering in January 2020, $112.6 million in proceeds from the private placement of shares of our convertible preferred stock, $140.0 million from the SFJ agreement, $20.0 million in proceeds from borrowings under a term loan facility with Silicon Valley Bank, and $7.0 million in proceeds from our issuance and sale of a promissory note. The amounts due and owed under the term loan facility and the promissory note have been repaid in full.

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 $51.0 million, $127.5 million and $304.7 million for the years ended December 31, 2017, 2018 and 2019, respectively. As of December 31, 2019, we had an accumulated deficit of $581.5 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 pegcetacoplan and APL-9, including our ongoing Phase 3 program in GA, our ongoing Phase 3 trials in PNH and our ongoing and planned clinical trials of pegcetacoplan in other indications; 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 are incurring additional costs associated with operating as a public company.

As of December 31, 2019, we had cash and cash equivalents of $352.0 million. We believe that our cash and cash equivalents as of December 31, 2019, together with the net proceeds of its follow-on public offering of $381.4 million in January 2020 and the $20.0 million received from SFJ in January 2020, will be sufficient to enable us to fund our current operations at least into mid-2021. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See “Liquidity and Capital Resources.”

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 within the next twelve months. 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 related to individuals performing research and development activities;
- 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 pegcetacoplan for intravitreal administration in geographic atrophy. We initiated a Phase 3 clinical program consisting of two Phase 3 clinical trials evaluating pegcetacoplan in patients with GA in September 2018, which we refer to as the DERBY and OAKS trials. We expect that both trials will be fully enrolled in the first half of 2020 and that we will announce data from these trials in mid-2021. In our Phase 2 clinical trial of pegcetacoplan in patients with GA, treatment with pegcetacoplan resulted in a significant reduction in the rate of GA lesion growth over 12 months.

PNH. We are developing pegcetacoplan as monotherapy for patients with PNH, administered by subcutaneous injection. We initiated the Phase 3 PEGASUS trial, an 80-patient randomized head-to-head study comparing pegcetacoplan monotherapy to eculizumab monotherapy in patients with PNH currently on treatment with eculizumab, in June 2018, completed enrollment in June 2019 and reported top-line results in January 2020. We plan to present detailed 16-week results from the PEGASUS trial at a future scientific meeting and expect to report 48-week topline data in the second half of 2020. In September 2019, we initiated our PRINCE trial, a 54-patient Phase 3 clinical trial in treatment-naïve patients. We expect to complete enrollment in this trial in the first half of 2020 and to present top-line data in the first quarter of 2021.

CAD. We are developing pegacetacoplan for patients with CAD, administered by subcutaneous injection. We initiated a Phase 2 clinical trial of pegcetacoplan in patients with CAD in the first quarter of 2018, reported interim data in December 2018 and provided additional data in June 2019. We intend to disclose our plans and timing for further clinical development of pegcetacoplan for patients with CAD in the first half of 2020.

C3G. We are developing pegcetacoplan for patients with glomerular diseases with complement involvement, administered by subcutaneous injection. We initiated a Phase 2 clinical trial of pegcetacoplan in patients with glomerular diseases with complement involvement, in the first quarter of 2018. We presented preliminary data on patients with C3G from this trial at the Annual Meeting of American Society of Nephropathy in November 2019. We intend to disclose our plans and timing for further clinical development of pegcetacoplan for patients with C3G in the first half of 2020

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 pegcetacoplan 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.

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 Note 2 in the notes to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, 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 over a time period equal to the expected term of our stock options at grant. 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. Before the IPO, we determined the expected term of our options utilizing the probability weighted time to liquidity event at each grant date, assuming that holders of our options would exercise at the time of such liquidity event. After the IPO, we calculate the expected term for options granted to employees based on the simplified method set forth in SEC Staff Accounting Bulletin 107, because it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate expected term due to the limited period of time its equity shares have been publicly traded. Under the simplified method, the weighted average vesting period is averaged with the contractual term of the option being valued. 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, from 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 on the date of grant.

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.

Convertible Notes

On September 16, 2019, we completed a private offering of Convertible Notes with an aggregate principal amount of $220.0 million.

The notes are convertible into shares of our common stock at an initial conversion rate of 25.3405 shares per $1,000 principal amount of the Convertible Notes (equivalent to an initial conversion price of approximately $39.46 per share of common stock). The conversion rate is subject to customary anti-dilution adjustments. In addition, following certain events that occur prior to the maturity date or if we deliver a notice of redemption, we are required to increase the conversion rate for a holder who elects to convert its notes in connection with such corporate event or a notice of redemption, as the case may be, in certain circumstances as provided in the Indenture. The Convertible Notes will also be subject to redemption at our option, on or after September 20, 2023, if certain conditions are met. The redemption price is equal to 100% of the principal amount of the notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date.

Pursuant to Accounting Standards Codification ("ASC") Subtopic 470-20 *Convertible Debt*, we used an effective interest rate of 10.5% to determine the liability component of the Convertible Notes. This resulted in the recognition of $145.1 million as the liability component of the notes and the recognition of the residual amount of $74.9 million as the debt discount with a corresponding increase to additional paid in capital for the equity component of the notes. Aggregate debt issuance costs of $7.1 million was allocated to the liability and equity components in the amounts of $4.7 million and $2.4 million, respectively.

Capped Call Transactions

On September 11, 2019, concurrently with the pricing of the Convertible Notes, we entered into capped call transactions with two counterparties. The capped call transactions are expected generally to reduce the potential dilution to our common stock upon any conversion of notes and/or offset any cash payments we are required to make in excess of the principal amount of the Convertible Notes, as the case may be, in the event that the market price per share of our common stock, as measured under the terms of the capped call transactions, is greater than the strike price of the capped call transactions, which is initially $39.4625 (the conversion price of the Convertible Notes) and is subject to anti-dilution adjustments substantially similar to those applicable to the conversion rate of such notes. If, however, the market price per share of the Company's common stock, as measured under the terms of the capped call transactions, exceeds the cap price of the capped call transactions, which is initially $63.14 per share, there would nevertheless be dilution and/or there would not be an offset of such potential cash payments, in each case, to the extent that such market price exceeds the cap price of the capped call transactions.

Pursuant to ASC 815-40 *Derivatives and Hedging*, we determined that the capped call transactions should be classified as equity instruments and the capped call premium paid in the amount of $28.4 million was recorded as a reduction to additional paid-in capital.

Development Derivative Liability

Following regulatory approval by the FDA or the European Medicines Agency, or the EMA, for the use of pegcetacoplan as a treatment for PNH we will be obligated to pay SFJ an initial payment of up to $5.0 million (or a total of $10.0 million if regulatory approval is granted by the FDA and the EMA) and then up to an additional $226.0 million in the aggregate (or up to $452 million if regulatory approval is granted by the FDA and the EMA) in six additional annual payments with the majority of the payments being made from the third anniversary to the sixth anniversary of regulatory approval. Such payments will be proportionately adjusted in the event that the actual funding from SFJ is lower or greater than $120 million (including as a result of the payment of the Additional SFJ Funding but excluding the $20 million funding payment made under the SFJ amendment). Additionally, we granted a security interest in all of our assets, excluding intellectual property and license agreements to which we are a party. In connection with the grant of the security interest, we agreed to certain affirmative and negative covenants, including restrictions on our ability to pay dividends, incur additional debt or enter into licensing transactions with respect to its intellectual property, other than specified types of licenses.

The SFJ agreement is presented as a derivative liability on the consolidated balance sheet as of December 31, 2019. The liability was initially recorded at the value of the $60.0 million of aggregate cash received pursuant to the contractual terms, which was determined to have been fairly valued as a level 3 derivative. During 2019, we received an additional $60.0 million as we met additional milestones in the SFJ agreement. The SFJ agreement was remeasured quarterly in 2019 and finally at December 31, 2019 as a level 3 derivative, with the total change in fair value from the date of execution to December 31, 2019 of $14.8 million recorded in loss from remeasurement of development derivative liability on the consolidated income statement.

The derivative is valued using a scenario-based discounted cash flow method, whereby each scenario makes assumptions about the probability and timing of cash flows, and such cash flows are present valued using a risk-adjusted discount rate. The analysis is calibrated such that the value of the derivative as of the date of the SFJ agreement was consistent with an arm's-length transaction. Key inputs to the level 3 fair value model include (i) the probability and timing of achieving stated development goals to receive the

next tranches of funding, (ii) the probability and timing of achieving FDA and EMA approval, (iii) SFJ's cost of borrowing (8.0%), and (iv) our cost of borrowing (16.6%).

SFJ's implied cost of borrowing was 8.0% and our implied cost of borrowing was 16.6% as of the reporting date. These implied costs of borrowing were determined assuming the SFJ agreement was initially executed with arm's-length terms. If the SFJ agreement was instead not determined to be an arm's-length transaction, then implied discount rates could differ.

If actual results or events differ materially from the estimates, judgments and assumptions used by us in applying these policies, our reported financial condition and results of operations could be materially affected.

Results of Operations

Comparison of Years Ended December 31, 2018 and 2019

The following table summarizes our results of operations for the years ended December 31, 2018 and 2019, together with the dollar increase or decrease and percentage change in those items:

	Year Ended December 31,		Change	Change
	2018	2019	$	%
Operating expenses:				
Research and development	$ 105,285,576	$ 220,968,770	$ 115,683,194	109.9%
General and administrative	22,639,184	67,046,483	44,407,299	196.2
Operating loss	(127,924,760)	(288,015,253)	(160,090,493)	125.1
Loss on extinguishment of debt	—	(1,501,215)	(1,501,215)	100.0
Loss from remeasurement of development derivative liability	—	(14,839,000)	(14,839,000)	100.0
Interest expense	(2,512,956)	(5,284,610)	(2,771,654)	110.3
Interest income	2,960,771	5,108,779	2,148,008	72.5
Other expense, net	(25,249)	(175,314)	(150,065)	594.3
Net loss	$ (127,502,194)	$ (304,706,613)	$ (177,204,419)	139.0

Research and Development Expenses

The following table summarizes our research and development expenses incurred during the years ended December 31, 2018 and 2019, together with the dollar increase or decrease and percentage change in those items:

	Year Ended December 31,		Change	Change
	2018	2019	$	%
Clinical trial costs	$ 54,928,992	$ 96,038,981	$ 41,109,989	74.8%
Contract manufacturing	27,925,474	71,728,933	43,803,459	156.9
Pre-clinical study expenses	2,836,183	9,374,317	6,538,134	230.5
Compensation and related personnel costs	14,207,537	37,648,194	23,440,657	165.0
Other research and development costs	3,989,978	6,186,266	2,196,288	55.0
Device development expenses	1,397,412	(7,921)	(1,405,333)	(100.6)
Total research and development expenses	$ 105,285,576	$ 220,968,770	$ 115,683,194	109.9

Research and development expenses increased by $115.7 million to $221.0 million for the year ended December 31, 2019 from $105.3 million for the year ended December 31, 2018, an increase of 109.9%. The increase in research and development expenses was primarily attributable to an increase of $41.1 million in clinical trial costs associated with the preparation for and commencement of our Phase 3 clinical trials, an increase of $43.8 million in manufacturing expenses in connection with the supply of pegcetacoplan for our Phase 3 clinical trials, an increase of $23.5 million in compensation and related personnel costs primarily due to the hiring of additional personnel in 2019, an increase of $6.5 million related to preclinical study expenses, and an increase of $2.2 million in research and development supporting activities and offset by a decrease of $1.4 million in device development expenses. We expect our research and development expenses to continue to increase as the number of patients in our trials increases and the number of ongoing trials increases.

General and Administrative Expenses

General and administrative expenses increased by $44.4 million to $67.0 million for the year ended December 31, 2019, from $22.6 million for the year ended December 31, 2018, an increase of 196.2%. The increase in general and administrative expenses was primarily attributable to an increase in employee related costs of $21.0 million due to the hiring of additional personnel, an increase in professional and consulting fees of $20.2 million, an increase in office, travel and related costs of $2.1 million, an increase of $1.5 million in information technology expenses and an increase in insurance costs of $0.6 million. These increases were offset by a decrease in license agreement costs of $1.0 million from the payment of certain milestones met in 2018. The increased employee related costs of $21.0 million consisted of $12.7 million related to an increase in salaries and benefits primarily due to the hiring of additional members of our management team, $6.3 million related to stock option expense associated with the grants of stock options to employees and $2.0 million in recruitment expense. The increased professional and consulting fees of $20.2 million primarily consisted of an increase in consulting fees of $16.7 million, an increase of $2.0 million in legal fees, an increase in communication and public relations fees of $0.9 million, an increase of $0.5 million in accounting fees, and an increase of $0.1 million in public company costs.

Loss on Extinguishment of Debt

On March 26, 2019, we repaid all outstanding amounts due and owed, including applicable termination fees, under our term loan facility with Silicon Valley Bank. The final payment included the outstanding balance of the term loan as well as (i) a prepayment fee contractually owed of $0.1 million, (ii) a final payment equal to 8% of the original principal amount of the term loan, or $1.6 million, and (iii) per diem interest of $0.1 million, for a total payment of $21.8 million, which resulted in a loss on extinguishment of debt of $1.2 million. On September 16, 2019, we repaid outstanding amounts due and owed on the promissory note with Golda Darty Partners, S.A. or GDP. The remaining discount on the promissory note related to the issuance of warrants in connection with the issuance of the promissory note resulted in a loss on extinguishment of debt of $0.3 million.

Loss from Remeasurement of Development Derivative Liability

Loss from remeasurement of development derivative liability was $14.8 million for the year ended December 31, 2019. On February 28, 2019, we entered into the SFJ agreement under which SFJ agreed to provide funding to us to support the development of pegcetacoplan for the treatment of patients with PNH. The SFJ agreement was amended on June 7, 2019 to provide for additional funding and we received $20.0 million upon execution of the SFJ amendment in June 2019. In each of June and September 2019, we achieved a $20.0 million development milestone under the terms of the agreement, result in receipt of an aggregate of $40.0 million of additional funding from SFJ. The change in fair value of the derivative liability is due to the remeasurement at December 31, 2019 which resulted in a loss of $14.8 million for the year ended December 31, 2019. The derivative liability was remeasured as a level 3 derivative.

Interest Expense

Interest expense was $5.3 million for the year ended December 31, 2019, an increase of $2.8 million, compared to $2.5 million for the year ended December 31, 2018. The increase in interest expense was primarily attributable to the amortization of the discount on the Convertible Notes offset by the decrease in interest expense attributable to our long-term debt under the term loan facility that we repaid in March 2019 and the promissory note that we repaid in 2019.

Interest Income

Interest income was $5.1 million for the year ended December 31, 2019, an increase of $2.1 million, compared to $3.0 million for the year ended December 31, 2018. The increase in interest income earned in 2019 from 2018 was due to the interest earned on our cash and cash equivalents that increased from the receipt of proceeds from of our follow-on offering in March 2019, the payments to us under the SFJ agreement and the receipt of proceeds from the Convertible Notes offering in September 2019.

Other Expense, Net

Other expense increased $0.2 million for the year ended December 31, 2019 as compared to the year ended December 31, 2018. The increase was primarily related to corporate franchise taxes and fees.

Comparison of Years Ended December 31, 2017 and 2018

The following table summarizes our results of operations for the years ended December 31, 2017 and 2018, together with the dollar increase or decrease and percentage change in those items:

	Year Ended December 31,		Change	Change
	2017	2018	$	%
Operating expenses:				
Research and development	$ 40,303,878	$ 105,285,576	$ 64,981,698	161.2%
General and administrative	10,463,151	22,639,184	12,176,033	116.4
Operating loss	(50,767,029)	(127,924,760)	(77,157,731)	152.0
Interest expense	(374,749)	(2,512,956)	(2,138,207)	570.6
Interest income	277,834	2,960,771	2,682,937	965.7
Other expense, net	(142,150)	(25,249)	116,901	(82.2)
Net loss	$ (51,006,094)	$ (127,502,194)	$ (76,496,100)	150.0

Research and Development Expenses

The following table summarizes our research and development expenses incurred during the years ended December 31, 2017 and 2018, together with the dollar increase or decrease and percentage change in those items:

	Year Ended December 31,		Change	Change
	2017	2018	$	%
Clinical trial costs	$ 15,231,683	$ 54,928,992	$ 39,697,309	260.6%
Contract manufacturing	13,323,343	27,925,474	14,602,131	109.6
Pre-clinical study expenses	1,699,902	2,836,183	1,136,281	66.8
Compensation and related personnel costs	4,933,207	14,207,537	9,274,330	188.0
Other research and development costs	3,659,506	3,989,978	330,472	9.0
Device Development Expenses	1,456,237	1,397,412	(58,825)	(4.0)
Total research and development expenses	$ 40,303,878	$ 105,285,576	$ 64,981,698	161.2

Research and development expenses increased by $65.0 million to $105.3 million for the year ended December 31, 2018 from $40.3 million for the year ended December 31, 2017, an increase of 161.2%. The increase in research and development expenses was primarily attributable to an increase of $39.7 million in clinical trial costs associated with the preparation for and commencement of our Phase 3 clinical trials of pegcetacoplan, an increase of $14.6 million in manufacturing expenses in connection with the supply for our Phase 3 clinical trials of pegcetacoplan, an increase of $9.3 million in compensation and related personnel costs primarily due to increased headcount in 2018, an increase of $1.1 million related to preclinical study expenses, and an increase of $0.3 million in research and development supporting activities, offset by a slight decrease of $0.1 million in device development expenses.

General and Administrative Expenses

General and administrative expenses increased by $12.2 million to $22.6 million for the year ended December 31, 2018, from $10.5 million for the year ended December 31, 2017, an increase of 116.4% The increase in general and administrative expenses was primarily attributable to an increase in employee related costs of $5.9 million due to the hiring of additional personnel, an increase in professional and consulting fees of $3.2 million, an increase in license agreement costs of $1.0 million, an increase in insurance costs of $0.8 million, an increase of $0.6 million in information technology expenses, and an increase in office, travel and related costs of $0.7 million. The increased employee related costs of $5.9 million consisted of $3.6 million related to an increase in salaries and benefits primarily due to the hiring of additional members of our management team, $1.4 million related to stock option expense associated with the grants of stock options to employees and $0.9 million in recruitment expense. The increased professional and consulting fees of $3.2 million primarily consisted of an increase of $1.0 million in legal fees, an increase of $0.9 million in accounting fees, an increase of $0.9 million in public company costs and an increase in consulting fees of $0.4 million.

Interest Expense

Interest expense was $2.5 million for the year ended December 31, 2018, an increase of $2.1 million, compared to $0.4 million for the year ended December 31, 2017. The increase in interest expense was attributable to interest expense incurred on our loan facility with Silicon Valley Bank and our promissory note with GDP.

Interest Income

Interest income was $3.0 million for the year ended December 31, 2018, an increase of $2.7 million, compared to $0.3 million for the year ended December 31, 2017. The increase in interest income earned in 2018 from 2017 was due to the interest earned on our cash and cash equivalents that increased from the completion of our IPO in November 2017 and the follow-on offering in April 2018.

Other Expense, Net

Other income, net increased $0.1 million for the year ended December 31, 2018 as compared to the year ended December 31, 2017. The increase was primarily related to corporate franchise taxes and fees.

Liquidity and Capital Resources

Sources of Liquidity

On November 13, 2017, we issued and sold 10,714,000 shares of common stock in our IPO at a public offering price of $14.00 per share for net proceeds of $137.2 million after deducting underwriting discounts and commissions of $10.5 million and other offering expenses of approximately $2.3 million. On November 13, 2017, upon the closing of the IPO, all shares of preferred stock then outstanding converted into an aggregate of 30,070,034 shares of common stock. In addition, on December 13, 2017, we issued and sold an additional 981,107 shares of common stock at the IPO price of $14.00 per share pursuant to the underwriters' partial exercise of their option to purchase additional shares of common stock, resulting in net proceeds of approximately $12.8 million, after underwriting discounts and commissions of $1.0 million.

On April 23, 2018, we issued and sold 5,500,000 shares of our common stock in a follow-on public offering at a public offering price of $25.50 per share for net proceeds of $131.3 million, after deducting underwriting discounts and commissions of $8.4 million and offering expenses of $0.5 million.

On March 11, 2019, we issued and sold 6,900,000 shares of our common stock in a follow-on offering at a public offering price of $17.00. We received net proceeds of $109.6 million after deducting underwriting discounts and commissions of $7.0 million and offering costs of $0.7 million.

On September 16, 2019, we completed a private offering of $220.0 million aggregate principal amount of Convertible Notes. We received net proceeds of approximately $212.9 million after deducting the initial purchasers' discounts and commissions and offering costs of $7.1 million. Prior to the IPO and the 2018 follow-on offering, we financed our operations primarily through $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 GDP.

Prior to the IPO, we financed our operations primarily through $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 GDP.

Subsequent to December 31, 2019, on January 13, 2020, we issued and sold 10,925,000 shares of our common stock in a follow-on offering at a public offering price of $37.00, including 1,425,000 shares sold pursuant to the underwriters' exercise in full of their option to purchase additional shares of common stock. We received total net proceeds of $381.4 million after deducting underwriting discounts and commissions of $22.2 million and offering costs of approximately $0.6 million.

Agreement with SFJ

On February 28, 2019, we entered into the SFJ agreement, under which SFJ agreed to provide funding to us to support the development of pegcetacoplan for the treatment of patients with PNH. Pursuant to the agreement, SFJ paid us $60.0 million following the signing of the agreement, and has agreed to pay us up to an additional $60.0 million in the aggregate in three equal installments upon the achievement of specified development milestones with respect to our Phase 3 program for pegcetacoplan in PNH and subject to our having cash resources at the time sufficient to fund at least 10 months of our operations. In addition, upon the mutual agreement between us and SFJ, at any time after the earlier of the date that we have reviewed the primary endpoint data from its PEGASUS Phase 3 trial of pegcetacoplan in patients with PNH and March 31, 2020, SFJ may fund an additional $50.0 million of our development costs.

On June 7, 2019, we amended the funding agreement with SFJ. Under the amendment, SFJ agreed to make an additional $20.0 million of funding payment to us to support the development of pegcetacoplan for the treatment of patients with PNH. This additional $20.0 million was in addition to and not part of the Additional SFJ Funding.

On June 27, 2019, we received $40.0 million from SFJ, consisting of $20.0 million as the first installment of the additional $60.0 million upon the achievement of a milestone and the $20.0 million payable under the SFJ amendment. On September 23, 2019, we received $20.0 million from SFJ as the second installment of the additional $60.0 million due to the achievement of a milestone. We met the remaining development milestones under the SFJ agreement upon the announcement of the PEGASUS Phase 3 trial data in January 2020. The remaining $20.0 million was paid in January 2020.

Following regulatory approval by the U.S. Food and Drug Administration, or the FDA, or the European Medicines Agency, or the EMA, for the use of pegcetacoplan as a treatment for PNH we will be obligated to pay SFJ an initial payment of up to $5.0 million (or a total of $10.0 million if regulatory approval is granted by the FDA and the EMA) and then up to an additional $226.0 million in the aggregate (or up to $452.0 million if regulatory approval is granted by the FDA and the EMA) in six additional annual payments with the majority of the payments being made from the third anniversary to the sixth anniversary of regulatory approval. Such payments will be proportionately adjusted in the event that the actual funding from SFJ is lower or greater than $120.0 million (including as a result of the payment of the Additional SFJ Funding but excluding the $20.0 million funding made under the SFJ amendment). Additionally, we granted a security interest in all of our assets, excluding intellectual property and license agreements to which we are a party. In connection with the grant of the security interest, we agreed to certain affirmative and negative covenants, including restrictions on our ability to pay dividends, incur additional debt or enter into licensing transactions with respect to its intellectual property, other than specified types of licenses.

Indebtedness

Term Loan Facility

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 accrued interest at a floating rate per annum equal to the WSJ prime rate plus 1.50%. Under the agreement, we were required to make monthly interest-only payments through November 1, 2019 and we were required to make 24 equal monthly payments of principal, plus accrued interest, thereafter from November 1, 2019 through October 1, 2021, when all unpaid principal and interest were to become due and payable.

On March 26, 2019, we repaid all outstanding amounts due and owed, including applicable termination fees, under the term loan facility. The final payment included the outstanding balance of the term loan as well as (i) a prepayment fee contractually owed of $0.1 million, (ii) a final payment equal to 8% of the original principal amount of the term loan, or $1.6 million, and (iii) per diem interest of $0.1 million, for a total payment of $21.8 million, which resulted in a loss on extinguishment of debt of $1.2 million.

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 had a ten-year term and included 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 could require us to repurchase the warrant for a total aggregate purchase price of $250,000. Silicon Valley Bank exercised the warrant in the fourth quarter of 2019.

Promissory Note

On October 19, 2017, we issued and sold an unsecured promissory note in the principal amount of $7.0 million to GDP. The note accrued interest at a rate per annum of 8.0% and was due and payable quarterly in arrears on the 19th day of each April, July, October and January. The promissory note had a maturity date of October 19, 2022. The promissory note was contractually subordinated to our obligations to SFJ under the SFJ agreement. On September 16, 2019, we repaid outstanding amounts due and owed, under the promissory note.

In connection with the issuance and sale of the $7.0 million promissory note, we issued 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 $0.4 million as a discount to the promissory note. This amount was being accreted as additional interest expense over the term of the promissory note. Upon the repayment of the promissory note, this discount resulted in a loss on extinguishment of debt of $0.3 million.

Convertible Notes

On September 16, 2019, we completed a private offering of Convertible Notes with an aggregate principal amount of $220.0 million. The Convertible Notes are senior unsecured obligations and bear interest at a rate of 3.5% per year payable semiannually in arrears on March 15 and September 15 of each year, beginning on March 15, 2020. The Convertible Notes will mature on September 15, 2026, unless earlier converted, redeemed or repurchased in accordance with their terms.

The net proceeds from the sale of the Convertible Notes were approximately $212.9 million after deducting the initial purchasers' discounts and commissions and estimated offering expenses payable. We used $28.4 million of the net proceeds from the sale of the Convertible Notes to pay the cost of the capped call transactions described below.

The Convertible Notes are convertible into shares of our common stock at an initial conversion rate of 25.3405 shares per $1,000 principal amount of Convertible Notes (equivalent to an initial conversion price of approximately $39.46 per share of common stock). The conversion rate is subject to customary anti-dilution adjustments. In addition, following certain events that occur prior to the maturity date or if we deliver a notice of redemption, we will increase the conversion rate for a holder who elects to convert its Convertible Notes in connection with such corporate event or a notice of redemption, as the case may be, in certain circumstances as provided in the Indenture.

Prior to March 15, 2026, the Convertible Notes are convertible only upon the occurrence of certain events. On or after March 15, 2026 until the close of business on the second scheduled trading day immediately preceding the maturity date of the Convertible Notes, holders may convert the Convertible Notes at any time. Upon conversion of the Convertible Notes, we will pay or deliver, as the case may be, cash, shares of our common stock or a combination of cash and shares of common stock, at our election.

Prior to September 20, 2023, we may not redeem the Convertible Notes. We may redeem for cash all or a portion of the Convertible Notes, at our option, on or after September 20, 2023 if the last reported sale price of our common stock has been at least 130% of the conversion price then in effect for at least 20 trading days (whether or not consecutive), including the trading day immediately preceding the date on which we provide a notice of redemption, during any 30 consecutive trading day period ending on, and including, the trading day immediately preceding the date on which we provide notice of redemption. The redemption price will be equal to 100% of the principal amount of the Convertible Notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date.

If we undergo a "fundamental change," as defined in the Indenture, prior to maturity, subject to certain conditions, holders may require us to repurchase for cash all or any portion of their Convertible Notes at a fundamental change repurchase price equal to 100% of the principal amount of the Convertible Notes to be repurchased, plus any accrued and unpaid interest to, but excluding, the fundamental change repurchase date.

The Indenture contains customary terms and covenants, including that upon certain events of default occurring and continuing, either the Trustee or the holders of at least 25% in principal amount of the outstanding Convertible Notes may declare 100% of the principal of, and accrued and unpaid interest, if any, on, all the Convertible Notes to be due and payable.

On September 11, 2019, concurrently with the pricing of the Convertible Notes, we entered into capped call transactions with two counterparties. The capped call transactions are expected generally to reduce the potential dilution to our common stock upon any conversion of Convertible Notes and/or offset any cash payments we are required to make in excess of the principal amount of converted Convertible Notes, as the case may be, in the event that the market price per share of our common stock, as measured under the terms of the capped call transactions, is greater than the strike price of the capped call transactions, which is initially $39.4625 (the conversion price of the Convertible Notes) and is subject to anti-dilution adjustments substantially similar to those applicable to the conversion rate of such Convertible Notes. If, however, the market price per share of our common stock, as measured under the terms of the capped call transactions, exceeds the cap price of the capped call transactions, which is initially $63.14 per share, representing a premium of 100% above the last reported sale price of $31.57 per share of our common stock on The Nasdaq Global Select Market on September 11, 2019, there would nevertheless be dilution and/or there would not be an offset of such potential cash payments, in each case, to the extent that such market price exceeds the cap price of the capped call transactions.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2017, 2018 and 2019:

	Year Ended December 31,		
	2017	**2018**	**2019**
Net cash used in operating activities	$ (46,595,073)	$ (131,240,797)	$ (211,135,445)
Net cash used in investing activities	—	—	(1,693,322)
Net cash provided by financing activities	197,375,114	131,903,360	388,541,484
Effect of exchange rate changes on cash and cash equivalents	—	(38,426)	4,702
Net increase (decrease) in cash and cash equivalents	$ 150,780,041	$ 624,137	$ 175,717,419

Net Cash Used in Operating Activities

Net cash used in operating activities was $211.1 million for the year ended December 31, 2019 and consisted primarily of a net loss of $304.7 million adjusted for $40.4 million of non-cash items, including share-based compensation expense of $21.1 million, a loss from remeasurement of development derivative liability of $14.8 million, and a loss on early extinguishment of debt of $1.5 million, a net increase in accounts payable, accrued expenses and other liabilities of $48.7 million and a net decrease in operating assets of $4.5 million. The net increase in operating liabilities resulted primarily from an increase in accrued expenses of $50.5 million.

Net cash used in operating activities was $131.2 million for the year ended December 31, 2018 and consisted primarily of a net loss of $127.5 million adjusted for non-cash items of $8.3 million, including share-based compensation expense of $7.7 million, and a net increase in operating assets of $12.0 million, which resulted primarily from an increase in prepaid assets of $19.3 million, offset by an increase in accounts payable of $6.6 million and an increase in accrued expenses of $2.2 million.

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 assets 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 Investing Activities

Net cash used in investing activities during the year ended December 31, 2019 was $1.7 million due to the purchase of fixed assets for our offices. There was no cash used in investing activities during the years ended December 31, 2018 and December 31, 2017.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $388.5 million during the year ended December 31, 2019 and consisted primarily of proceeds from the issuance of the Convertible Notes in September 2019 of $212.9 million, the issuance of common stock in our March follow-on offering of $109.6 million, the receipt of $120.0 million from the SFJ agreement and $3.1 million upon the exercise of stock options, offset by $28.7 million for the repayment of our term loan facility and promissory note, and $28.4 million for capped call premiums paid.

Net cash provided by financing activities was $131.9 million during the year ended December 31, 2018 and consisted primarily of proceeds from the issuance of common stock in the follow-on public offering that we completed in April 2018.

Net cash provided by financing activities was $197.4 million during the year ended December 31, 2017. 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 option to purchase additional shares of common stock 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.

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 our cash and cash equivalents as of December 31, 2019, together with the net proceeds of its follow-on public offering of $381.4 million in January 2020 and the $20.0 million received from SFJ in January 2020 will enable us to fund our operating expenses and capital expenditure requirements at least into mid-2021. 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 our existing cash and cash equivalents will be sufficient to enable us to complete all of our ongoing and planned Phase 3 clinical trials of pegcetacoplan or to complete the development of pegcetacoplan or any of our other product candidates. Because of the numerous risks and uncertainties associated with the development of pegcetacoplan 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 pegcetacoplan, APL-9 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;
- our ability to enter into, and the terms and timing of, any collaborations, licensing or other arrangements;
- 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, 2019:

	Payments Due by Period				
	Total	Less than 1 Year	1-3 Years	3-5 Years	More than 5 Years
Convertible Notes (1)	273,878,611	7,700,000	15,400,000	15,400,000	235,378,611
Non-cancellable purchase commitments	35,300,000	35,300,000	—	—	—
Operating Leases (2)	17,679,804	3,679,786	6,605,527	6,090,976	1,303,515
Total	$ 326,858,415	$ 46,679,786	$ 22,005,527	$ 21,490,976	$ 236,682,126

(1) Amounts include interest on long-term debt represents obligations under the debt outstanding as of December 31, 2019, applying contractual fixed interest rate and assuming scheduled payments are paid as contractually required through maturity.

(2) 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.

On February 28, 2019, we entered into the SFJ agreement. Under the SFJ agreement, following regulatory approval by the FDA or the EMA of the use of pegcetacoplan as a treatment for PNH, we will be obligated to pay SFJ an initial payment of up to $5.0 million (or a total of $10 million if regulatory approval is granted by the FDA and the EMA) and then up to an additional $226.0 million in the aggregate (or $452.0 million if regulatory approval is granted by the FDA and the EMA) in six additional annual payments with the majority of the payments being made from the third anniversary to the sixth anniversary of regulatory approval. Such payments will be proportionately adjusted in the event that the actual funding from SFJ is lower or greater than $120.0 million (including as a result of the payment of the Additional SFJ Funding but excluding the $20.0 million funding made under the SFJ amendment). The timing and likelihood of such payments are not currently known.

During the third quarter of 2019, we entered into contracts to conduct research and development activities with third parties which commit us to pay future milestone payments up to $15.0 million or to pay royalty fees ranging from 3-6% if any of the research results in regulatory approval or commercial revenue for a product. The scope of the services under the research and development contracts can be modified and the contracts cancelled by us upon written notice. In some instances, the contracts may be cancelled by the third party upon written notice. If we were to cancel these contracts, we would be required only to pay for activities incurred through termination date. 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 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 pegcetacoplan. 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. In 2018 we made one milestone payment of $0.4 million under the nonophthalmic license. 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. In 2018 we made one milestone payment, net of credits for the annual maintenance payment, of $0.7 million under the ophthalmic license. 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 either the contracts are cancelable at any time by us, generally upon 30 days prior written notice to the CRO, or the noncancelable minimum purchase commitments under such contracts have already

been satisfied, and therefore we believe that our non-cancelable obligations under these agreements are not material. Under these agreements, as of December 31, 2019, we are obligated to pay up to $1.8 million 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.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. As of December 31, 2019, we had cash and cash equivalents of $352.0 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.

Item 8. Financial Statements and Supplementary Data.

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 sheet of Apellis Pharmaceuticals, Inc. (the Company) as of December 31, 2018, the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity and cash flows for each of the two years in the period ended December 31, 2018, 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, 2018, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

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 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. 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 served as the Company’s auditor from 2015 to 2019.

Boston, Massachusetts

February 26, 2019

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of Apellis Pharmaceuticals, Inc.

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheet of Apellis Pharmaceuticals, Inc. and subsidiaries (the "Company") as of December 31, 2019, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows, for the year ended December 31, 2019, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2019, and the results of its operations and its cash flows for the year ended December 31, 2019, in conformity with accounting principles generally accepted in the United States of America.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2019, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated February 27, 2020 expressed an unqualified opinion on the Company's internal control over financial reporting.

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 audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the US federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit 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. Our audit 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 audit 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 audit provides a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current-period audit of the financial statements that was communicated or required to be communicated to the audit committee and that (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Development Derivative Liability — Refer to Notes 5 and 9 to the financial statements

Critical Audit Matter Description

On February 28, 2019, the Company entered into a development funding agreement with SFJ Pharmaceuticals Group (“SFJ”) under which SFJ agreed to provide funding to the Company to support the development of one of the Company’s clinical trials (“SFJ Agreement”). The SFJ Agreement is presented as a derivative liability whose fair value is based on unobservable inputs. The liability is initially recorded at the value of the aggregate cash received pursuant to the contractual terms and is subsequently remeasured at each quarter with the change in fair value recorded in loss from remeasurement of development derivative liability on the income statement.

We identified the valuation of the development derivative liability as a critical audit matter. The development derivative liability is valued using a scenario-based discounted cash flow method, whereby each scenario makes assumptions about the probability and timing of cash flows, and such cash flows are present valued using a risk-adjusted discount rate. This model includes unobservable inputs including the probability and timing of achieving U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) approval. This required a high degree of auditor judgment and an increased extent of effort, including the need to involve our fair value specialists.

How the Critical Audit Matter Was Addressed in the Audit

Our audit procedures related to the development derivative liability model and unobservable inputs used by management to estimate the fair value of the development derivative liability included the following, among others:

- We tested the effectiveness of controls over management's valuation of the development derivative liability, such as those related to management's assumptions over the probability and timing of achieving FDA and EMA approval.
- We evaluated the reasonableness of management's assumptions over the probability and timing of achieving FDA and EMA approval by comparing the assumptions within the model to:
  - Internal communications to management and the Board of Directors.
  - Information included in the Company's press releases, as well as in analyst reports for the Company.
  - Inquiries with those responsible for clinical affairs regarding the progress of ongoing trials.
- With the assistance of our fair value specialists, we evaluated the reasonableness of the valuation methodology by testing the source information and the mathematical accuracy of the calculation.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
February 27, 2020

We have served as the Company's auditor since 2019.

APELLIS PHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS

	December 31,	
	2018	**2019**
Assets		
Current assets:		
Cash and cash equivalents	$ 176,267,666	$ 351,985,085
Prepaid assets	24,333,851	19,802,008
Other current assets	1,837,704	1,307,591
Total current assets	202,439,221	373,094,684
Non-current Assets:		
Right-of-use assets	—	14,110,209
Property and equipment, net	977,918	1,654,999
Other assets	116,420	385,088
Total assets	$ 203,533,559	$ 389,244,980
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 10,254,938	$ 8,360,527
Accrued expenses	5,103,002	54,782,951
Current portion of long-term-debt	1,666,667	—
Current portion of operating lease liabilities	—	2,609,341
Total current liabilities	17,024,607	65,752,819
Long-term liabilities:		
Convertible Senior Notes	—	142,566,851
Development derivative liability	—	134,839,000
Term loan facility	18,722,321	—
Promissory note	6,655,193	—
Operating lease liabilities	—	11,856,634
Other liabilities	158,783	—
Total liabilities	42,560,904	355,015,304
Stockholders' equity:		
Preferred stock, $0.0001 par value; 10,000,000 shares authorized and zero shares issued and outstanding at December 31, 2018 and 2019	—	—
Common stock, $0.0001 par value; 200,000,000 shares authorized and at December 31, 2018 and 2019; 56,279,307 and 63,938,003 shares issued and outstanding at December 31, 2018 and 2019, respectively	5,628	6,393
Additional Paid-in capital	437,855,681	615,849,518
Accumulated other comprehensive loss	(122,807)	(153,775)
Accumulated deficit	(276,765,847)	(581,472,460)
Total stockholders' equity	160,972,655	34,229,676
Total liabilities and stockholders' equity	$ 203,533,559	$ 389,244,980

See accompanying notes to consolidated financial statements

APELLIS PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

	Year Ended December 31,		
	2017	2018	2019
Operating expenses:			
Research and development	$ 40,303,878	$ 105,285,576	$ 220,968,770
General and administrative	10,463,151	22,639,184	67,046,483
Operating loss	(50,767,029)	(127,924,760)	(288,015,253)
Loss on extinguishment of debt	—	—	(1,501,215)
Loss from remeasurement of development derivative liability	—	—	(14,839,000)
Interest expense	(374,749)	(2,512,956)	(5,284,610)
Interest income	277,834	2,960,771	5,108,779
Other expense, net	(142,150)	(25,249)	(175,314)
Net loss	(51,006,094)	(127,502,194)	(304,706,613)
Other comprehensive loss:			
Foreign currency loss	—	(122,807)	(30,968)
Total other comprehensive loss	—	(122,807)	(30,968)
Comprehensive loss, net of tax	$ (51,006,094)	$ (127,625,001)	$ (304,737,581)
Net loss per common share, basic and diluted	$ (3.68)	$ (2.34)	$ (4.90)
Weighted-average number of common shares used in net loss per common share, basic and diluted	13,870,949	54,396,483	62,228,601

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 Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Outstanding Shares	Amount	Outstanding Shares	Amount				
Balance at January 1, 2017	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
Issuance of common stock in follow-on offering, net of offering costs	—	—	5,500,000	550	131,193,480	—	—	131,194,030
Issuance of common stock upon exercise of stock options	—	—	445,155	45	727,465	—	—	727,510
Share-based compensation expense	—	—	—	—	7,733,256	—	—	7,733,256
Net loss	—	—	—	—	—	—	(127,502,194)	(127,502,194)
Foreign currency loss	—	—	—	—	—	(122,807)	—	(122,807)
Balance at December 31, 2018	—	—	56,279,307	5,628	437,855,681	(122,807)	(276,765,847)	160,972,655
Issuance of common stock in follow-on offering, net of offering costs	—	—	6,900,000	690	109,580,418	—	—	109,581,108
Issuance of common stock upon exercise of stock options or warrants	—	—	758,696	75	3,129,355	—	—	3,129,430
Recognition of equity component of convertible notes	—	—	—	—	72,520,035	—	—	72,520,035
Purchase of capped call transactions and associated costs	—	—	—	—	(28,380,000)	—	—	(28,380,000)
Share-based compensation expense	—	—	—	—	21,144,029	—	—	21,144,029
Net loss	—	—	—	—	—	—	(304,706,613)	(304,706,613)
Foreign currency loss	—	—	—	—	—	(30,968)	—	(30,968)
Balance at December 31, 2019	—	$ —	63,938,003	$ 6,393	$ 615,849,518	$ (153,775)	$ (581,472,460)	$ 34,229,676

See accompanying notes to consolidated financial statements

APELLIS PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year Ended December 31,		
	2017	2018	2019
Operating Activities			
Net loss	$ (51,006,094)	$ (127,502,194)	$ (304,706,613)
Adjustments to reconcile net loss to net cash used in operating activities:			
Share-based compensation expense	5,418,710	7,733,256	21,144,029
Loss on early extinguishment of debt	—	—	1,501,215
Loss from remeasurement of development derivative liability	—	—	14,839,000
Non-cash lease expense	—	—	355,766
Depreciation expense	—	—	239,683
Amortization of debt discounts	—	—	51,725
Amortization of discounts for promissory note	13,563	71,791	—
Amortization of term loan facility discounts	11,935	582,043	104,172
Amortization of discounts for convertible notes, net of financing costs	—	—	2,186,014
Changes in operating assets and liabilities:			
Prepaid assets	(3,927,155)	(299,006)	4,531,039
Other current assets	50,443	(19,275,118)	287,353
Other assets	10,177	(309,361)	(322,789)
Accounts payable	(51,622)	(978,188)	(1,640,774)
Accrued expenses	932,299	6,587,469	50,453,518
Other liabilities	1,952,671	2,148,511	(158,783)
Net cash used in operating activities	(46,595,073)	(131,240,797)	(211,135,445)
Investing Activities			
Purchase of property and equipment	—	—	(1,693,322)
Net cash used in investing activities	—	—	(1,693,322)
Financing Activities			
Issuance of Series E convertible preferred stock, net of issuance costs	19,747,847	—	—
Deferred issuance costs	—	(18,180)	—
Proceeds from issuance of term loan, net of issuance costs	19,795,007	—	—
Proceeds from issuance of promissory note, net of issuance costs	6,569,840	—	—
Proceeds from issuance of common stock, net of issuance costs	150,062,959	131,194,030	109,581,108
Proceeds from development derivative liability	—	—	120,000,000
Payments for capped call transactions and associated costs	—	—	(28,380,000)
Proceeds from issuance of convertible notes, net of issuance costs	—	—	212,912,238
Proceeds from issuance of stock options and warrants	520,760	—	—
Proceeds from exercise of stock options and warrants	678,701	727,510	3,129,430
Repayment of promissory note	—	—	(7,000,000)
Repayment of term loan facility	—	—	(21,701,292)
Net cash provided by financing activities	197,375,114	131,903,360	388,541,484
Effect of exchange rate changes on cash and cash equivalents	—	(38,426)	4,702
Net increase in cash and cash equivalents	150,780,041	624,137	175,717,419
Cash and cash equivalents at beginning of period	24,863,488	175,643,529	176,267,666
Cash and cash equivalents at end of period	$ 175,643,529	$ 176,267,666	$ 351,985,085
Supplemental Disclosure of Non-Cash Financing Activities			
Conversion of convertible preferred stock to common stock	$ 111,802,773	$ —	$ —
Cash paid for interest	$ 134,167	$ 1,816,333	$ 987,377
Equity component of convertible notes	$ —	$ —	$ 72,520,035

See accompanying 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 Waltham, Massachusetts, effective January 1, 2020. Prior to that date, the Company's principal offices were 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").

Convertible Notes Offering

On September 16, 2019, the Company completed a private offering of $220,000,000 aggregate principal amount of 3.5% convertible senior notes due 2026 (the "Convertible Notes").

The net proceeds from the sale of the Convertible Notes were approximately $212,912,000 after deducting the initial purchasers' discounts and commissions of $6,600,000 and offering expenses of $487,763 paid by the Company. The Company used $28,380,000 of the net proceeds from the sale of the Convertible Notes to pay the cost of the capped call transactions described below in Note 7.

On September 16, 2019, the Company entered into an indenture (the "Indenture") with respect to the Convertible Notes with U.S. Bank National Association, as trustee (the "Trustee"). The Convertible Notes are senior unsecured obligations of the Company and bear interest at a rate of 3.5% per year payable semiannually in arrears on March 15 and September 15 of each year, beginning on March 15, 2020. The Convertible Notes will mature on September 15, 2026, unless converted earlier, redeemed or repurchased in accordance with the terms of the Convertible Notes. See Note 7 – Long-term Debt for additional information.

Development Derivative Liability

On February 28, 2019, the Company entered into a development funding agreement with SFJ Pharmaceuticals Group ("SFJ") under which SFJ agreed to provide funding to the Company to support the development of pegcetacoplan for the treatment of patients with paroxysmal nocturnal hemoglobinuria ("PNH"). Pursuant to the agreement, SFJ paid the Company $60,000,000 following the signing of the agreement, and agreed to pay the Company up to an additional $60,000,000 in the aggregate in three equal installments upon the achievement of specified development milestones with respect to the Company's Phase 3 program for pegcetacoplan in PNH and subject to the Company having cash resources at the time sufficient to fund at least ten months of the Company's operations. In addition, upon the mutual agreement of the Company and SFJ, at any time after the earlier of the date that the Company has reviewed the primary endpoint data from its PEGASUS Phase 3 trial of pegcetacoplan in patients with PNH and March 31, 2020, SFJ may fund an additional $50,000,000 of the Company's development costs (the "Additional SFJ Funding").

On June 7, 2019, the Company and SFJ amended the development funding agreement (the "SFJ amendment"). Under the SFJ amendment, SFJ agreed to make an additional $20,000,000 funding payment to the Company to support the development of pegcetacoplan for the treatment of patients with PNH. This additional $20,000,000 payment is in addition to and not part of the Additional SFJ Funding.

On June 27, 2019, the Company received $40,000,000 from SFJ, consisting of $20,000,000 as the first installment of the additional $60,000,000 upon the achievement of a milestone and the $20,000,000 payable under the SFJ amendment.

On September 23, 2019, the Company received $20,000,000 from SFJ as the second installment of the additional $60,000,000 upon the achievement of a milestone.

The Company met the remaining development milestone under the SFJ agreement upon the Company's announcement of the primary endpoint data from its PEGASUS Phase 3 trial on January 7, 2020 and the final installment of $20,000,000 of the additional $60,000,000 was paid on January 29, 2020.

Follow-on Public Offering

On March 11, 2019, the Company issued and sold 6,900,000 shares of its common stock at a price per share of $17.00 in a follow-on public offering ("2019 follow-on offering"). The Company received net proceeds of approximately $109,581,000 after deducting underwriting discounts and commissions of approximately $7,038,000 and offering costs of $680,891.

On April 23, 2018, the Company issued and sold 5,500,000 shares of its common stock at a price per share of $25.50 in a follow-on public offering. The Company received net proceeds of $131,324,477 after deducting underwriting discounts and commissions of $8,415,000 and offering costs of $509,973.

Liquidity and Going Concern

The accompanying consolidated financial statements have been prepared on the basis of the realization of assets and the satisfaction of liabilities and commitments in the normal course of business. Subsequent to December 31, 2019, on January 13, 2020, the Company issued and sold 10,925,000 shares of its common stock at a price per share to the public of $37.00 in a follow-on public offering, including an additional 1,425,000 shares of its common stock that were sold at the follow-on public offering price of $37.00 per share pursuant to the underwriters' in full exercise of their option to purchase additional shares of common stock. The Company received net proceeds of approximately $381,374,000 from the sale of shares in the follow on offering after deducting underwriting discounts and commissions of approximately $22,233,000 and offering costs of approximately $618,000. As of February 27, 2020, the date of issuance of these consolidated financial statements, the Company believes that its cash and cash equivalents as of December 31, 2019 of $351,985,085, together with the net proceeds of its follow-on offering of approximately $381,374,000 in January 2020 and the $20,000,000 received from SFJ in January 2020, will be sufficient to fund its operations and capital expenditures for at least the next twelve months from the date of issuance of these consolidated financial statements. The Company's future viability beyond that point is dependent on its ability to raise additional capital to finance its operations.

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.

There are 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. If the Company is not able to obtain the required funding for its operations, or is not able to obtain funding on terms that are favorable to the Company, it could be forced to delay, reduce or eliminate its research and development programs or future commercialization efforts and its business could be materially harmed.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries, Apellis Australia Pty Ltd, Apellis Switzerland GmbH, Apellis Ireland Ltd., and Apellis MA Securities, Inc. 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 2019 presentation.

Offering Costs

Offering costs represent underwriting, legal, accounting and other direct costs related to the Company's follow-on offerings and filing of a registration statements on Form S-3 in 2018 and 2019, and related to the Company's offering of Convertible Notes in 2019. Costs were deferred until completion of the follow-on offerings and offering of Convertible Notes, at which time they were reclassified to additional paid-in capital as a reduction of the proceeds. Deferred issuance costs related to the registration statement on Form S-3 that the Company filed in January 2020 have been capitalized and will be reclassified to additional paid-in capital as a reduction of the proceeds at the time when shares are issued. The Company does not consider these amounts material at December 31, 2019.

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 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, development derivative liability, accrued expenses, prepaid expenses and convertible debt.

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

The Company is required to disclose information on the fair value of financial instruments and inputs that enable an assessment of the fair value. The three levels of the fair value hierarchy prioritize valuation inputs based upon the observable nature of those inputs as follows:

Level 1 – Quoted prices in active markets for identical assets or liabilities;

Level 2 – Inputs other than quoted prices included within level 1 that are observable for the asset or liability, either directly or indirectly;

Level 3 – Unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability.

The Company's financial instruments, in addition to those presented in Note 7, Long-term Debt and Note 9, Fair Value Measurements, include cash and cash equivalents, the Australian research and development credit, accounts payable and accrued liabilities. Management believes that the carrying amounts of cash and cash equivalents, the Australian research and development credit, accounts payable and accrued expenses approximate the fair value due to the short-term nature of those instruments.

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 the fair value. As of December 31, 2018 and 2019, the Company had assets consisting of cash and cash equivalents held in banks outside of the United States of approximately $121,600 and $1,598,300, respectively.

Foreign Currency

The financial position and results of operations of the Company's Australian and Swiss subsidiaries are measured using the foreign subsidiary's local currency. Revenues and expenses of the subsidiaries have been translated into U.S. dollars at average exchange rates prevailing during the period from January 1, 2019 through December 31, 2019. Assets and liabilities have been translated at the rates of exchange on the balance sheet date. The resulting translation gain and loss adjustments are recorded directly as a separate component of stockholders' equity. Prior to August 1, 2018, when the functional currency of the Company's Australian subsidiary was changed from the U.S. dollar to the Australian dollar, the transactions with the Australian subsidiary were recorded in U.S. dollars and were not translated.

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.

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.

Patents

Costs incurred in connection with the application for and issuance of patents are expensed as incurred.

Income Taxes

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, 2018 and 2019, the Company did not have any significant uncertain tax positions.

Share-based Compensation

The Company recognizes all share-based payments to employees, including grants of employee stock options, in the statements of operations and comprehensive loss based on their estimated fair values over the requisite service periods for each award. The Company remeasures the fair value of share-based awards to non-employees 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 believes the group selected has sufficient similar economic and industry characteristics. Before the IPO, 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. After the IPO, the Company calculates the expected term for options granted to employees based on the "simplified" method set forth in SEC Staff Accounting Bulletin 107, because it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term due to the limited period of time its equity shares have been publicly traded. Under the simplified method, the weighted average vesting period is averaged with the contractual term of the option being valued. 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 cash equivalents are the only financial instruments that potentially subject the Company to concentrations of credit risk. Cash and cash equivalents are held at financial institutions in the United States, Australia and Switzerland. The Company is exposed to credit risk in the event of default by the financial institution to the extent that cash and cash equivalent balances recorded in the balance sheets are in excess of the amounts that are insured by the Federal Deposit Insurance Corporation. The Company has not experienced any losses on its deposits since inception, and management believes that minimal credit risk exists with respect to these financial institutions.

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 notes 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's components of comprehensive loss other than its net loss, are the foreign currency gains/losses recorded from the remeasurement of the long term intra-entity loan transaction to the Company's wholly owned subsidiaries as well as the foreign currency gain/ loss from the translation of the Company's wholly owned subsidiaries into U.S. dollars in 2018 and 2019. These components are a result of the change in the Australian subsidiary's functional currency to Australian dollars effective August 1, 2018 and the creation of the Swiss subsidiary in 2019.

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 was 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 had no impact on its consolidated financial statements.

In January 2016, the FASB issued ASU No. 2016-01, *Financial Instruments – Overall*, amending several elements surrounding the recognition and measurement of financial instruments and requiring equity investments (except those accounted for under the equity method of accounting or those that result in consolidation) to be measured at fair value with changes in fair value recognized in net income. Effective January 1, 2018, the Company adopted this ASU on a prospective basis. The adoption did not have a material impact on its consolidated financial statements and related disclosures.

In February 2016, the FASB issued ASU 2016-02 *Leases (Topic 842)* which establishes a right-of-use ("ROU") model that requires a lessee to record a ROU asset and a lease liability on the consolidated balance sheet for all leases with terms longer than twelve months. Leases will be either classified as finance or operating, with classification affecting the pattern of expense recognition in the income statement. ASU 2016-02 also requires significant additional disclosures about the amount, timing and uncertainty of cash flows from leases. The Company adopted ASU 2016-02 effective January 1, 2019 using a modified retrospective method and will not restate comparative periods. As permitted under the guidance, the Company carried forward the assessment of whether contracts contain or are leases, the classification of leases and remaining terms. The Company recognized $5,511,865 of ROU assets and operating lease liabilities, primarily relating to office space leases, on the consolidated balance sheet upon adoption. During 2019, the Company leased additional office space resulting in an initial recognition value of $9,838,982 of ROU assets and operating lease liabilities.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement – Disclosure Framework*, that modifies the disclosure requirements with respect to fair value measurements. Among the changes, entities will no longer be required to disclose the amount of and reasons for transfers between Levels 1 and 2 of the fair value hierarchy, but will be required to disclose the range and weighted average used to develop significant unobservable inputs for Level 3 fair value measurements. Effective January 1, 2018, the Company early adopted this ASU, which did not have a material impact on its consolidated financial statements and related disclosures.

3. Common Stock

The Company has reserved the following shares of common stock for future issuance:

	December 31,		
	2017	2018	2019
Shares reserved under 2010 Equity Incentive Plan	5,817,844	5,013,153	—
Shares reserved under 2017 Equity Incentive Plan	1,682,596	4,032,390	6,319,001
Shares reserved under 2017 Employee Stock Purchase Plan	468,823	972,164	972,164
Common stock warrants	14,064	14,064	—
Total	7,983,327	10,031,771	7,291,165

4. Convertible Preferred Stock

Authorized capital stock includes 10,000,000 shares of preferred stock at December 31, 2018 and 2019.

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.

5. Development Derivative Liability

On February 28, 2019, the Company entered into the SFJ agreement under which SFJ agreed to provide funding to the Company to support the development of pegcetacoplan for the treatment of patients with PNH. Pursuant to the agreement, SFJ paid the Company $60,000,000 following the signing of the agreement, and agreed to pay the Company up to an additional $60,000,000 in the aggregate in three equal installments upon the achievement of specified development milestones with respect to the Company's Phase 3 program for pegcetacoplan in PNH and subject to the Company having cash resources at the time sufficient to fund at least 10 months of the Company's operations. In addition, upon the mutual agreement of the Company and SFJ, at any time after the earlier of the date that the Company has reviewed the primary endpoint data from its PEGASUS Phase 3 trial of pegcetacoplan in patients with PNH and March 31, 2020, SFJ may fund an additional $50,000,000 of the Company's development costs.

On June 7, 2019, the Company and SFJ amended the development funding agreement. Under the SFJ amendment, SFJ agreed to make an additional $20,000,000 funding payment to the Company to support the development of pegcetacoplan for the treatment of patients with PNH. This additional $20,000,000 payment is in addition to and not part of the Additional SFJ Funding.

On June 27, 2019, the Company received $40,000,000 from SFJ, consisting of $20,000,000 as the first installment of the additional $60,000,000 upon the achievement of a milestone and the $20,000,000 payable under the SFJ amendment.

On September 23, 2019, the Company received $20,000,000 from SFJ as the second installment of the additional $60,000,000 upon the achievement of a milestone.

The Company met the remaining development milestone under the SFJ agreement upon the Company's announcement of the primary endpoint data from its PEGASUS Phase 3 trial on January 7, 2020 and the final installment of $20,000,000 of the additional $60,000,000 was paid on January 29, 2020.

Under the SFJ agreement following regulatory approval by the FDA or EMA for the use of pegcetacoplan as a treatment for PNH the Company will be obligated to pay SFJ an initial payment of up to $5,000,000 (or a total of $10,000,000 if regulatory approval is granted by the FDA and the EMA) and then up to an additional $226,000,000 in the aggregate (or up to $452,000,000 if regulatory approval is granted by the FDA and the EMA) in six additional annual payments with the majority of the payments being made from the third anniversary to the sixth anniversary of regulatory approval. Such payments will be proportionately adjusted in the event that the actual funding from SFJ is lower or greater than $120,000,000 (including as a result of the payment of the Additional SFJ Funding but excluding the $20,000,000 funding payment made under the SFJ amendment). Additionally, the Company granted a

security interest in all of its assets, excluding intellectual property and license agreements to which it is a party. In connection with the grant of the security interest, the Company agreed to certain affirmative and negative covenants, including restrictions on its ability to pay dividends, incur additional debt or enter into licensing transactions with respect to its intellectual property, other than specified types of licenses.

The SFJ agreement is presented as a derivative liability on the consolidated balance sheet as of December 31, 2019. The liability was initially recorded at the value of the $60,000,000 aggregate cash received pursuant to the contractual terms, which was determined to have been fair value, measured as a level 3 derivative. During 2019, the Company received an additional $60,000,000 under the SFJ agreement and the Company met additional milestones in the agreement. The derivative liability was remeasured quarterly at fair value in 2019 and finally at December 31, 2019 as a level 3 derivative, with the total change in fair value of $14,839,000 recorded for the year ended December 31, 2019 in loss from remeasurement of development derivative liability on the consolidated income statement. The remeasurement of the development derivative liability at December 31, 2019 resulted in a remeasured fair value of $134,839,000 as of December 31, 2019 on the consolidated balance sheet.

The following table presents a rollforward of the liability:

	Development Derivative Liability
Balance at fair market value, January 1, 2019	$ —
Amounts received under the SFJ agreement and SFJ amendment	120,000,000
Loss recorded in loss from remeasurement of development derivative liability	14,839,000
Balance at fair market value, December 31, 2019	$ 134,839,000

The derivative is valued using a scenario-based discounted cash flow method, whereby each scenario makes assumptions about the probability and timing of cash flows, and such cash flows are present valued using a risk-adjusted discount rate. The analysis is calibrated such that the value of the derivative as of the date of the SFJ agreement was consistent with an arm's-length transaction. Key inputs to the level 3 fair value model include (i) the probability and timing of achieving stated development milestones to receive the next tranches of funding, (ii) the probability and timing of achieving FDA and EMA approval, (iii) SFJ's cost of borrowing (8.0%), and (iv) the Company's cost of borrowing (16.6%).

SFJ's implied cost of borrowing was 8.0% and the Company's implied cost of borrowing was 16.6% as of the reporting date. These implied costs of borrowing were determined assuming the SFJ agreement was initially executed with arm's-length terms. If the SFJ agreement was instead not determined to be an arm's-length transaction, then implied discount rates could differ.

6. Accrued Expenses and Prepaid Assets

Accrued expenses are as follows:

	December 31, 2018	December 31, 2019
Accrued research and development	$ 3,481,570	$ 36,449,386
Accrued payroll liabilities	269,046	11,442,889
Other	1,352,386	6,890,676
Total	$ 5,103,002	$ 54,782,951

Prepaid assets include $23,053,511 and $18,102,049 of prepaid research and development costs as of December 31, 2018 and 2019, respectively.

7. Long-term Debt

Convertible Senior Notes

On September 16, 2019, the Company completed a private offering of Convertible Notes with an aggregate principal amount of $220,000,000 issued pursuant to an indenture (the "Indenture") with U.S. Bank National Association, as trustee (the "Trustee").

The net proceeds from the sale of the Convertible Notes were approximately $212,912,000 after deducting the initial purchasers' discounts and commissions of $6,600,000 and offering expenses of $487,763 paid by the Company. The Company used $28,380,000 of the net proceeds from the sale of the Convertible Notes to pay the cost of the capped call transactions described below.

The Convertible Notes are senior unsecured obligations of the Company and bear interest at a rate of 3.5% per year payable semiannually in arrears on March 15 and September 15 of each year, beginning on March 15, 2020. The Convertible Notes will mature on September 15, 2026, unless converted earlier, redeemed or repurchased in accordance with the terms of the Convertible Notes.

The Convertible Notes are convertible into shares of the Company's common stock at an initial conversion rate of 25.3405 shares per $1,000 principal amount of Convertible Notes (equivalent to an initial conversion price of approximately $39.4625 per share of common stock). The conversion rate is subject to customary anti-dilution adjustments. In addition, following certain events that occur prior to the maturity date or if the Company deliver a notice of redemption, the Company will increase the conversion rate for a holder who elects to convert its Convertible Notes in connection with such corporate event or a notice of redemption, as the case may be, in certain circumstances as provided in the indenture.

Prior to March 15, 2026, the Convertible Notes are convertible only upon the occurrence of certain events. On or after March 15, 2026 until the close of business on the second scheduled trading day immediately preceding the maturity date of the Convertible Notes, holders may convert the Convertible Notes at any time. Upon conversion of the Convertible Notes, the Company will pay or deliver, as the case may be, cash, shares of the Company's common stock or a combination of cash and shares of common stock, at the Company's election.

Prior to September 20, 2023, the Company may not redeem the Convertible Notes. The Company may redeem for cash all or a portion of the Convertible Notes, at its option, on or after September 20, 2023 if the last reported sale price of the Company's common stock has been at least 130% of the conversion price then in effect for at least 20 trading days (whether or not consecutive), including the trading day immediately preceding the date on which the Company provides a notice of redemption, during any 30 consecutive trading day period ending on, and including, the trading day immediately preceding the date on which the Company provides notice of redemption. The redemption price will be equal to 100% of the principal amount of the Convertible Notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date.

If the Company undergoes a "fundamental change," as defined in the Indenture, prior to maturity, subject to certain conditions, holders may require the Company to repurchase for cash all or any portion of their Convertible Notes at a fundamental change repurchase price equal to 100% of the principal amount of the notes to be repurchased, plus any accrued and unpaid interest to, but excluding, the fundamental change repurchase date.

Pursuant to Accounting Standards Codification ("ASC") Subtopic 470-20 *Convertible Debt*, the Company used an effective interest rate of 10.5% to determine the liability component of the Convertible Notes. This resulted in the recognition of $145,065,803 as the liability component of the Convertible Notes and the recognition of the residual amount of $74,934,197 as the debt discount with a corresponding increase to additional paid in capital for the equity component of the Convertible Notes. Aggregate debt issuance costs of $7,087,763 were allocated to the liability and equity components in the amounts of $4,673,600 and $2,414,162, respectively.

Interest expense for the Convertible Notes was $4,399,093 from inception through December 31, 2019, which included amortization of the discount on the Convertible Notes of $2,089,368, accrued semi-annual coupon payable of $2,224,445 and amortization of debt issuance costs of $85,280. As of December 31, 2019, $4,588,320 of debt issuance costs was recorded on the consolidated balance sheet as a reduction to the carrying amount of the Convertible Notes.

The aggregate balance of the Convertible Notes, net of unamortized debt issuance costs, as of December 31, 2019 is $142,566,851.

Capped Call Transactions

On September 11, 2019, concurrently with the pricing of the Convertible Notes, the Company entered into capped call transactions with two counterparties. The capped call transactions are expected generally to reduce the potential dilution to the Company's common stock upon any conversion of Convertible Notes and/or offset any cash payments the Company is required to make in excess of the principal amount of converted Convertible Notes, as the case may be, in the event that the market price per share of the Company's common stock, as measured under the terms of the capped call transactions, is greater than the strike price of the capped call transactions, which is initially $39.4625 (the conversion price of the Convertible Notes) and is subject to anti-dilution adjustments substantially similar to those applicable to the conversion rate of such Convertible Notes. If, however, the market price per share of the Company's common stock, as measured under the terms of the capped call transactions, exceeds the cap price of the capped call transactions, which is initially $63.14 per share, representing a premium of 100% above the last reported sale price of $31.57 per share of its common stock on The Nasdaq Global Select Market on September 11, 2019, there would nevertheless be dilution and/or there would not be an offset of such potential cash payments, in each case, to the extent that such market price exceeds the cap price of the capped call transactions.

Pursuant to ASC 815-40 *Derivatives and Hedging*, the Company determined that the capped call transactions should be classified as equity instruments and the capped call premium paid in the amount of $28,380,000 was recorded as a reduction to additional paid-in capital as of September 30, 2019.

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 $20,000,000 term loan facility (the "term loan facility"). Borrowings under the term loan facility accrued interest at a floating rate per annum equal to the WSJ prime rate plus 1.50%. Under the agreement, the Company was required to make monthly interest-only payments through November 1, 2019 and to make 24 equal monthly payments of principal, plus accrued interest, thereafter from November 1, 2019 through October 1, 2021, when all unpaid principal and interest would become due and payable.

On March 26, 2019, the Company voluntarily repaid all outstanding amounts due and owed, including applicable termination fees, under the term loan facility. The final payment of $21,802,403 totaled per diem interest of $101,111 and $21,701,292 for the outstanding balance of the term loan facility which included (i) a final payment equal to 8% of the original principal amount of the term loan facility of $1,600,000, and (ii) a prepayment fee contractually owed of $100,000 plus other fees of $1,292 which resulted in a total loss on extinguishment of debt of $1,208,132.

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 had 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 could require the Company to repurchase the warrant for a total aggregate purchase price of $250,000. The warrants were exercised in November 2019.

Related Party Promissory Note

On October 19, 2017, the Company issued and sold an unsecured promissory note in the principal amount of $7,000,000 to Golda Darty Partners S.A. ("GDP"), an affiliate of one of the Company's stockholders. The promissory note accrued interest at a rate per annum of 8.0%, and was due and payable quarterly in arrears on the 19th day of each April, July, October and January. The promissory note had a maturity date of October 19, 2022 when the $7,000,000 would be due and payable in its entirety. The promissory note was contractually subordinated to the Company's obligations to SFJ under the SFJ agreement.

On September 16, 2019, the Company voluntarily repaid all outstanding amounts due and owed under the promissory note, except for a small amount of interest subsequently repaid. The payment of $7,118,904 reflected per diem interest of $118,904 and $7,000,000 for the outstanding principal balance of the promissory note.

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 was being accreted as additional interest expense over the term of the promissory note. Upon the repayment of the promissory note, the Company recorded a loss on extinguishment of debt of $293,083 due to the remaining discount.

The contractual maturities of the Company's long-term debt obligations due subsequent to December 31, 2019 consist of the $220,000,000 Convertible Senior Notes which mature in September 2026.

8**. Leases**

On January 1, 2019, the Company adopted ASU 2016-02 *Leases (Topic 842)* using a modified retrospective method. The Company recognized $5,511,865 of lease assets and liabilities. There was no impact to retained earnings upon adoption of Topic 842. The underlying assets of the Company's leases primarily relate to office space leases, but also include some equipment leases. The Company determines if an arrangement qualifies as a lease at its inception. During 2019, the Company leased additional office space resulting in an initial recognition value of $9,838,982 of lease assets and liabilities.

As a practical expedient permitted under Topic 842, the Company has elected to account for the lease and non-lease components as a single lease component for all leases of which it is the lessee. Lease payments, which may include lease and non-lease components, are included in the measurement of the Company's lease liabilities to the extent that such payments are either fixed amounts or variable amounts that depend on a rate or index as stipulated in the lease contract. When the Company cannot readily determine the rate implicit in the lease, the Company determines its incremental borrowing rate by using the rate of interest that it would have to pay to borrow on a collateralized basis over a similar term, an amount equal to the lease payments in a similar economic environment.

The Company enters into lease agreements with terms generally ranging from 2-7 years. Some of the Company's lease agreements include Company options to extend the lease on a month to month basis or for set periods for up to five years. Many leases also include options to terminate the leases within one year or per other contractual terms. Renewal and termination options were generally not included in the lease term for the Company's existing operating leases.

As of December 31, 2019, all leases were classified as operating lease assets and liabilities. Operating lease assets were $14,110,209 and operating lease liabilities were $14,465,975 at December 31, 2019. At December 31, 2019, the weighted average remaining lease term of operating leases was 5.01 years and the weighted average discount rate used to measure the outstanding operating lease liabilities leases was 8.19%.

For the year ended December 31, 2019, the total lease cost for operating lease expense was approximately $2,369,000.

Supplemental cash flow information related to operating leases for the year ended December 31, 2019 is as follows:

Operating cash flows from operating leases	$	2,013,273
Right of use assets obtained in exchange for lease obligations	$	10,201,170

The maturity of the Company's operating lease liabilities as of December 31, 2019 are as follows:

2020	$	3,679,786
2021		3,336,325
2022		3,269,202
2023		3,287,748
2024 and thereafter		4,106,743
Total future minimum lease payments		17,679,804
Less imputed interest		(3,213,829)
Total operating lease liabilities	$	14,465,975

Rental expense under operating leases totaled $798,760 for the year ended December 31, 2018.

Under the previous lease accounting standard, ASC 840, *Leases*, future minimum rental payments for lease obligations with initial terms in excess of one year as of December 31, 2018 were as follows:

2019	$	1,251,720
2020		1,292,025
2021		975,750
2022		998,350
2023 and thereafter		2,341,219
Total	$	6,859,064

9. Fair Value Measurements

The Company is required to disclose information on the fair value of financial instruments and inputs that enable an assessment of the fair value. The three levels of the fair value hierarchy prioritize valuation inputs based upon the observable nature of those inputs as follows:

Level 1 – Quoted prices in active markets for identical assets or liabilities;

Level 2 – Inputs other than quoted prices included within level 1 that are observable for the asset or liability, either directly or indirectly;

Level 3 – Unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability.

The following table presents the fair value of financial instruments recorded originally at amortized cost or fair value and not re-measured on a recurring basis:

	December 31, 2018			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 92,355,167			$ 92,355,167
Total Financial Assets	$ 92,355,167	$ —	$ —	$ 92,355,167
Financial Liabilities:				
Term loan facility		$ 18,722,321		$ 18,722,321
Related party promissory note		7,401,203		7,401,203
Total Financial Liabilities	$ —	$ 26,123,524	$ —	$ 26,123,524

	December 31, 2019			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 281,314,069	-		$ 281,314,069
Total Financial Assets	$ 281,314,069	$ —	$ —	$ 281,314,069
Financial Liabilities:				
Convertible senior notes*			$ 149,496,359	149,496,359
Total Financial Liabilities	$ —	$ —	$ 149,496,359	$ 149,496,359

* The convertible notes were measured and recognized at fair value on the consolidated balance sheet at inception.

As of December 31, 2018, the fair value of the Company's promissory note was $7,401,203, based on discounted cash flows, market-based expectations for interest rates, credit risk and the contractual terms of the debt instrument. The Company paid interest on the term loan facility at a variable interest rate and accordingly the carrying amount approximated fair value at December 31, 2018.

As of December 31, 2019, the fair value of debt component of the Convertible Notes was $149,496,359, based on the discounted cash flows for comparable straight debt instrument. The Convertible Notes accrue a semi-annual coupon at an annual rate of 3.5%, which was included in accrued expenses in the consolidated balance sheet at December 31, 2019.

The following table presents the fair value of financial instruments recorded at fair value at inception and remeasured on a recurring basis:

	December 31, 2018			
	Level 1	Level 2	Level 3	Total
Financial Liabilities:				
Common stock warrant liability		$ 158,783		$ 158,783
Total Financial Liabilities	$ —	$ 158,783	$ —	$ 158,783

	December 31, 2019			
	Level 1	Level 2	Level 3	Total
Financial Liabilities:				
Development derivative liability			134,839,000	134,839,000
Total Financial Liabilities	$ —	$ —	$ 134,839,000	$ 134,839,000

The fair value of the SFJ agreement is presented as a derivative liability based on level 3 inputs. The derivative is valued using a scenario-based discounted cash flow method, whereby each scenario makes assumptions about the probability and timing of cash flows, and such cash flows are present valued using a risk-adjusted discount rate. The analysis is calibrated such that the value of the derivative as of the date of the SFJ agreement was consistent with an arm's-length transaction. Key inputs to the level 3 fair value model include (i) the probability and timing of achieving stated development milestones to receive the next tranches of funding, (ii) the probability and timing of achieving FDA and EMA approval, (iii) SFJ's cost of borrowing (8.0%), and (iv) the Company's cost of borrowing (16.6%). A 10% change in the key inputs of i) the probability and timing of payment and ii) the discount rate utilized would result in a change in fair value of the development derivative liability of approximately 13.3% or $17,886,000.

SFJ's implied cost of borrowing was 8.0% and the Company's implied cost of borrowing was 16.6% as of the reporting date. These implied costs of borrowing were determined assuming the SFJ agreement was initially executed with arm's-length terms.

The common stock warrant liability was valued based upon the underlying value of the Company's common stock.

10. 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.

In addition, the Company is also party to a 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. 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.

In 2018, the Company made payments of $1,025,000, net of a credit for the annual license maintenance payment, for the achievement of milestones under these agreements.

11. 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 2017, 2018 and 2019 the Company recorded $123,624, $322,459 and $806,915 respectively, for employer contributions made to the 401(k) Plan.

12. Refundable Research and Development Credits 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 components of loss from continuing operations before provision for income taxes are as follows:

	Year Ended December 31,		
	2017	2018	2019
Domestic	$(47,523,183)	$(122,900,285)	$(297,127,180)
Foreign	(3,482,911)	(4,601,909)	(7,579,433)
Total	$(51,006,094)	$(127,502,194)	$(304,706,613)

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, 2018 and 2019, 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.

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		2018		2019	
	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%	$(26,775,461)	21.0%	$(63,988,409)	21.0%
State income taxes, net of federal benefit	(1,634,924)	3.3	(6,397,993)	5.0	(16,423,857)	5.4
Change in valuation allowances	11,176,291	(20.8)	38,156,506	(29.9)	90,300,408	(29.6)
Re-measurement of deferred taxes	15,659,916	(31.9)	—	—	—	—
Tax credits	(3,316,729)	7.7	(6,149,021)	4.8	(6,113,296)	2.0
Change in state apportionment, Kentucky tax reform and other	—	—	873,508	(0.7)	(16,861)	0.0
Permanent and other	(4,032,421)	6.7	292,461	(0.2)	(3,757,985)	1.2
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,	
	2018	2019
Deferred tax assets:		
Intangible assets	$ 19,616	$ 15,519
Share-based compensation	2,914,583	6,624,638
Deferred interest expense	135,585	—
Contribution carryforwards	36,759	41,409
Net operating loss carryforwards	64,296,165	102,623,330
Research and development credits	7,269,624	14,476,348
Orphan drug credits	7,165,354	9,380,475
Development derivative liability	—	35,874,491
Accruals	—	2,259,190
Other	—	11,250
Total deferred tax assets	81,837,686	171,306,650
Deferred tax liabilities:		
Accrual to cash adjustment	(2,463,715)	—
Unrealized gain	(12,094)	—
Convertible debt	—	(11,479,891)
481(a) adjustment	—	(2,891,490)
Total deferred tax liabilities	(2,475,809)	(14,371,381)
Net deferred tax assets before allowance:	79,361,877	156,935,269
Less valuation allowance	(79,361,877)	(156,935,269)
Net deferred tax assets	$ —	$ —

At December 31, 2018, the Company had approximately $251,388,000 and $254,631,000 of Federal and state net operating loss carryforward, respectively. At December 31, 2019, the Company had approximately $392,878,000 and $358,345,000 of Federal and state net operating loss carryforwards, respectively. The Company also had $24,163,000 of federal research and development tax credit carryforwards as of December 31, 2019. 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.

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 $99,955,000 of Federal and State NOLs and $24,163,000 of Federal and State research & development tax credit carryforwards. Of the $99,955,000 of Federal and State NOLs, approximately $10,716,000 is limited under Section 382. Of the $24,163,000 of Federal and State tax credit carryforwards, approximately $1,892,000 is limited under Section 383. Subsequent ownership changes may further affect the limitation in future years.

The Company's estimate of the realizability of the deferred tax asset is dependent on its estimate of projected future levels of taxable income. In analyzing future taxable income levels, the Company considered all evidence currently available, both positive and negative. Based on its analysis, the Company recorded a valuation allowance for deferred tax assets, net of deferred tax liabilities, as of December 31, 2018 and 2019.

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 $15,659,916. 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 Company has completed its assessment of the U.S. Tax Reform Act and has determined no additional impacts during 2018.

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.

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, 2018, or 2019.

The Company files income tax returns in the U.S. federal jurisdiction, and applicable state jurisdictions and in Australia’s and Switzerland’s federal jurisdiction. The Company’s earliest tax years open and subject to examination by taxing authorities are 2016, for the U.S. federal jurisdiction, and 2015, for U.S. states’ and Australia’s federal jurisdiction. Federal and state net operating losses are subject to review by taxing authorities in the year utilized.

13. Commitments and Contingencies

The Company has entered into a leasing agreement for lab space in Watertown, Massachusetts with an estimated commencement date of June 2, 2020 (the “Lab Lease”). The Lab Lease has a term of 85 months and includes leasing 9,704 square feet of office space. The Lab Lease provides for initial monthly lease payments of $58,224 per month. The base rent payable over the lease period is $5,425,279.

The Company contracts to conduct research and development activities with third parties. Certain of these contracts commit the Company to pay future milestone payments up to $15,000,000 or to pay royalty fees ranging from 3-6% if any of the research results in regulatory approval or commercial revenue for a product. 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. If the Company were to cancel these contracts as of December 31, 2019, the Company would be required to pay certain termination costs and other fees of approximately $1,789,000 that would be incurred in future periods.

As of December 31, 2019, the Company has non-cancellable purchase commitments for 2020 with certain manufacturing vendors in the amount of approximately $35,300,000.

The Company also has certain payment and other obligations under the SFJ agreement, which are discussed above in Note 5.

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 not 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.

14. 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.

Additionally, during 2019 and thereafter, the Company has granted equity awards as equity inducement awards material to entry into employment with the Company to certain newly hired employees outside of the Company's existing plans in accordance with Nasdaq listing rule 5635(c)(4).

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.

Under the Executive Separation Benefits and Retention Plan and by resolutions adopted by the Compensation Committee in October 2019, the stock options granted to the Company's executives and employees will become fully vested upon the occurrence of a change in control, as defined in the Executive Separation Benefits and Retention Plan, if such executive or employee is terminated without cause or resigns for good reason within 12 months after such change in 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 Option	Weighted - Average Contractual Life (in years)	Aggregate Intrinsic Value
Outstanding, December 31, 2017	6,355,581	4.78	2.66	7.64	107,534,863
Granted	2,060,685	15.86	13.13	—	—
Exercised	(468,263)	2.61	1.46	—	4,953,187
Forfeited	(450,269)	6.58	4.27	—	—
Outstanding, December 31, 2018	7,497,734	8.09	5.52	7.31	45,706,169
Granted	4,365,520	21.15	17.31	—	—
Exercised	(747,136)	3.85	2.81	—	15,659,119
Forfeited	(261,681)	12.67	10.34	—	—
Outstanding, December 31, 2019	10,854,437	13.52	10.43	7.59	185,847,165
Options exercisable, December 31, 2019	4,808,730	6.94	4.62	5.82	113,868,890
Expected to vest, December 31, 2019	6,045,707	18.76	15.04	9.01	71,978,275

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 fair value of the common stock as of December 31, 2019. Estimated fair values of the common stock at the time of the grants between May 12, 2010 and the Company's IPO in November 2017 were between $1.71 and $14.00. Actual fair market values of the Company's common stock from the time of the IPO through December 31, 2019 were between $11.47 and $32.18. The fair market value of options vested during the years ended December 31, 2018 and 2019 were $5,062,428 and $12,906,436, respectively.

Total share-based compensation expense during the years ended was as follows:

	Year Ended December 31,		
	2017	2018	2019
Research and development	$ 2,678,956	$ 3,559,047	$ 10,682,553
General and administrative	2,739,754	4,174,209	10,461,476
Total share-based compensation expense	$ 5,418,710	$ 7,733,256	$ 21,144,029

At December 31, 2017, 2018 and 2019, unrecognized compensation expense related to unvested options, was $10,415,787, $27,266,206 and $79,291,036, respectively, which the Company expects to recognize over an estimated weighted-average period of 3.14, 2.99, and 3.24 years, respectively.

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,		
	2017	2018	2019
Risk-free interest rate	1.21 - 2.30%	2.68 - 2.99%	1.42 - 2.56%
Dividend yield	0%	0%	0%
Volatility	51.6 - 55.8%	87.0 - 110.9%	102.6 - 111.2%
Expected terms (years)	5.3 - 7.0	5.94 - 6.25	5.31 - 6.08

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 common stock. The number of shares of 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 common stock, (ii) 1.0% of the number of shares of common stock outstanding on the first day of the fiscal year and (iii) an amount determined by the board of directors. The board of directors initiated the first offering under the ESPP in October 2019.

15. Net Loss per Common Share

The following table presents the calculation of basic and diluted net loss per common share:

	Year Ended December 31,		
	2017	2018	2019
Numerator:			
Net loss	$ (51,006,094)	$ (127,502,194)	$ (304,706,613)
Denominator:			
Weighted-average number of common shares used in net loss per common share -- basic and diluted	13,870,949	54,396,483	62,228,601
Net loss per common share -- basic and diluted	$ (3.68)	$ (2.34)	$ (4.90)

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,		
	2017	2018	2019
Common stock under option	6,355,581	7,497,734	10,854,437
Common stock warrants	14,064	14,064	—
Total	6,369,645	7,511,798	10,854,437

16. Related Party Transaction

Effective as of May 1, 2018, the Company entered into a subscription license agreement and a services agreement with Revon Systems, Inc. (“Revon”). Under the subscription license agreement, Revon granted the Company an exclusive license to use the Revon software platform and applications for any purpose with respect to the Company's programs in age-related macular degeneration, hemolytic diseases and complement-dependent nephropathies for an annual license fee of $175,000 and an option to obtain a perpetual, exclusive license thereafter for $350,000. Under the services agreement, Revon provided development services with respect to the Revon software to the Company for $250,000 during the first year. Prior to the acquisition of Revon by an unrelated third party in July 2019, the Company paid the remainder of the annual license fee due for the second year, exercised the option for the perpetual license and discontinued the services agreement. For the year ended December 31, 2019, the Company paid Revon a total of $691,667.

Each of Cedric Francois, the Company’s chief executive officer, Pascal Deschatelets, the Company’s chief operating officer, and Alec Machiels, a member of the board of directors, was an affiliate of Revon. The Board approved the Revon agreements after review by a subcommittee of the disinterested members of the Board and determination by the full Board that the terms of the Revon agreements were fair, reasonable and in the best interests of the Company. The exercise of the option for the perpetual license was approved in accordance with the Company’s related party transaction policy.

17. Selected Quarterly Financial Data (Unaudited)

The following interim financial information presents the Company's 2018 and 2019 results of operations on a quarterly basis:

	Quarter Ended			
	March 31, 2018	June 30, 2018	September 30, 2018	December 31, 2018
Operating Loss	$ (21,438,145)	$ (33,485,442)	$ (35,804,581)	$ (37,196,592)
Net Loss	(21,736,304)	(33,334,300)	(35,972,115)	(36,459,475)
Net Loss per common share, basic and diluted (1)	(0.43)	(0.61)	(0.64)	(0.65)

	Quarter Ended			
	March 31, 2019	June 30, 2019	September 30, 2019	December 31, 2019
Operating Loss	$ (48,650,570)	$ (63,476,438)	$ (69,947,962)	$ (105,940,283)
Net Loss	(50,574,367)	(71,090,164)	(69,824,659)	(113,217,423)
Net Loss per common share, basic and diluted (1)	(0.87)	(1.12)	(1.10)	(1.77)

(1) The sum of the four quarters of earnings per share for 2018 and 2019 may not add to the full year earnings per share amount due to rounding and/or the use of quarter-to-date weighted average shares to calculate the earnings per share amount in each respective quarter.

18. Subsequent Events

On January 13, 2020, the Company issued and sold 10,925,000 shares of its common stock at a price per share to the public of $37.00 in a follow-on public offering, including an additional 1,425,000 shares of its common stock that were sold at the follow-on public offering price of $37.00 per share pursuant to the underwriters' in full exercise of their option to purchase additional shares of common stock. The Company received net proceeds of approximately $381,374,000 after deducting underwriting discounts and commissions of approximately $22,232,000 and offering costs of approximately $618,000 for these transactions.

The Company received the final $20,000,000 from the SFJ development funding agreement on January 29, 2020.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

The Company's management, with the participation of the Company's chief executive officer and chief financial officer, evaluated the effectiveness of the Company's disclosure controls and procedures as of as of December 31, 2019. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of the Company's disclosure controls and procedures as of December 31, 2019, the Company's chief executive officer and chief financial officer concluded that, as of such date, the Company's disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control Over Financial Reporting

The management of the Company is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rule 13a-15(f) or 15d-15(f) under the Exchange Act. Our internal control over financial reporting is a process designed by, or under the supervision of, the company's principal executive and principal financial officers and effected by the company's board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the Company;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the Company; and
- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

The company's management assessed the effectiveness of the company's internal control over financial reporting as of December 31, 2019. In making this assessment, the Company's management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control-Integrated Framework (2013).

Based on our assessment, management concluded that, as of December 31, 2019, the Company's internal control over financial reporting is effective based on those criteria.

Deloitte & Touche LLP, the Company's independent auditors have issued an audit report on our assessment of the company's internal control over financial reporting, which is included below.

Changes in Internal Control over Financial Reporting

As required by Rule 13a-15(d) of the Exchange Act, our management, including our principal executive officer and our principal financial officer, conducted an evaluation of the internal control over financial reporting to determine whether any changes occurred during the year ended December 31, 2019 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting. Based on that evaluation, our principal executive officer and principal financial officer concluded no such changes during the year ended December 31, 2019 materially affected, or were reasonably likely to materially affect, our internal control over financial reporting.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of Apellis Pharmaceuticals, Inc.

Opinion on Internal Control over Financial Reporting

We have audited the internal control over financial reporting of Apellis Pharmaceuticals, Inc. and subsidiaries (the "Company") as of December 31, 2019, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2019, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by COSO.
We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated financial statements as of and for the year ended December 31, 2019, of the Company and our report dated February 27, 2020, expressed an unqualified opinion on those financial statements.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.
/s/ Deloitte & Touche LLP
Boston, Massachusetts
February 27, 2020

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Information required by this item will be contained in our definitive proxy statement to be filed with the Securities and Exchange Commission on Schedule 14A in connection with our 2020 Annual Meeting of Stockholders, or the Proxy Statement, which we intend to file not later than 120 days after the end of our fiscal year ended December 31, 2019, under the headings “Information about our Executive Officers,” “Election of Directors,” “Corporate Governance,” and “ Section 16(a) Beneficial Ownership Reporting Compliance,” and is incorporated in this Annual Report on Form 10-K by reference.

We have adopted a Code of Business Conduct and Ethics that applies to our officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions, which is available on our website at www.apellis.com. The Code of Business Conduct and Ethics is intended to qualify as a “code of ethics” within the meaning of Section 406 of the Sarbanes-Oxley Act of 2002 and Item 406 of Regulation S-K. In addition, we intend to promptly disclose the nature of any amendment to our Code of Business Conduct and Ethics or any waiver from our Code of Business Conduct and Ethics granted to any officer or director on our website or in a current report on Form 8-K.

Item 11. Executive Compensation.

The information required by this item regarding executive compensation will be set forth in the sections titled “Executive Compensation” and “Director Compensation” in our Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this item regarding security ownership of certain beneficial owners and management will be set forth in the sections titled “Security Ownership of Certain Beneficial Owners and Management” and “Equity Compensation Plan Information” in our Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this item regarding certain relationships and related transactions and director independence will be set forth in the sections titled “Certain Relationships and Related Party Transactions,” “Election of Directors,” and “Corporate Governance,” respectively, in our Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this item regarding principal accountant fees and services will be set forth in the section titled “Principal Accountant Fees and Services” in our Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) Documents filed as a part of this Report:

(1) Financial Statements—Included in Item 8 of this Annual Report on Form 10-K.

(2) Financial Statement Schedules

No financial statement schedules have been filed as part of this Annual Report on Form 10-K because they are not applicable, not required or the required information is otherwise included in our consolidated financial statements or notes thereto.

(3) Index to Exhibits.

Exhibit Index

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewtih
		Form	File Number	Date of Filing	Exhibit Number	
2.1*	Asset Purchase Agreement	S-1	333-220941	10/13/2017	2.1	
3.1	Restated Certificate of Incorporation of the Registrant	8-K	001-38276	11/13/2017	3.1	
3.2	Amended and Restated By-Laws of the Registrant	8-K	001-38276	11/13/2017	3.2	
4.1	Specimen Stock Certificate evidencing the shares of common stock	S-1/A	333-220941	10/27/2017	4.1	
4.2	Investors' Rights Agreement dated as of August 7, 2017, among the Registrant and the other parties thereto	S-1	333-220941	10/13/2017	4.2	
4.3	Indenture (including form of Note), dated as of September 16, 2019, by and between Apellis Pharmaceuticals, Inc. and U.S. Bank National Association, as trustee	8-K	001-38276	9/16/2019	4.1	
4.4	Description of Securities Registered Under Section 12 of the Exchange Act					X
10.1+	2010 Equity Incentive Plan, as amended	S-1	333-220941	10/13/2017	10.1	
10.2+	Form of Incentive Stock Option Grant Notice and Agreement under 2010 Equity Incentive Plan	S-1	333-220941	10/13/2017	10.2	
10.3+	Form of Nonstatutory Stock Option Grant Notice and Agreement under 2010 Equity Incentive Plan	S-1	333-220941	10/13/2017	10.3	
10.4+	2017 Stock Incentive Plan	S-1/A	333-220941	10/30/2017	10.4	
10.5+	Form of Incentive Stock Option Agreement under 2017 Stock Incentive Plan	S-1/A	333-220941	10/27/2017	10.5	
10.6+	Form of Nonstatutory Stock Option Agreement under 2017 Stock Incentive Plan	S-1/A	333-220941	10/27/2017	10.6	
10.7+	Form of Director and Officer Indemnification Agreement	S-1/A	333-220941	10/27/2017		
10.8†	Patent License Agreement, dated as of March 28, 2008, by and between Apellis AG and The Trustees of the University of Pennsylvania, as assigned to the Registrant	S-1/A	333-220941	10/13/2017	10.8	
10.9†	Amended and Restated Patent License Agreement, dated as of March 28, 2008, by and between Potentia Pharmaceuticals, Inc. and The Trustees of the University of Pennsylvania, as amended by the First Amendment to the Amended and Restated Patent License Agreement, dated as of October 14, 2009 and as assigned to the Registrant	S-1/A	333-220941	10/13/2017	10.9	
10.10†	Office Lease Agreement, dated as of October 21, 2010, by and between the Registrant and DHB Properties, LLC, as amended	S-1/A	333-220941	10/13/2017	10.1	
10.11	Summary of Non-Employee Director Compensation Program	S-1/A	333-220941	10/30/2017	10.11	
10.12	Lease, dated as of April 27, 2017, by and between the Registrant and NWALP PHOP Property Owner, LLC	S-1/A	333-220941	10/13/2017	10.13	
10.13+	2017 Employee Stock Purchase Plan	S-1/A	333-220941	10/30/2017	10.15	
10.14+	Offer Letter, dated as of October 9, 2017, by and between the Registrant and Timothy Sullivan	S-1/A	333-220941	10/20/2017	10.16	
10.15+	Warrant to purchase shares of common stock issued to Golda Darty Partners S.A.	S-1/A	333-220941	10/20/2017	10.17	
10.16	Warrant to purchase shares of common stock issued to Silicon Valley Bank	S-1/A	333-220941	10/20/2017	10.18	
10.17	Loan and Security Agreement, dated as of October 20, 2017, between the Registrant and Silicon Valley Bank	S-1/A	333-220941	10/20/2017	10.19	
10.18	Fourth Addendum to Office Lease Agreement, dated as of July 2, 2018, by and between Registrant and Westwind Way Properties, LLC.	10-Q	001-38276	7/31/2018	10.1	

10.19	First Amendment to Lease, dated July 25, 2018, by and between Registrant and NWALP PHOP Property Owner LLC.	10-Q	001-38276	7/31/2018	10.2	
10.20	Second Amendment to Lease, dated June 5, 2019, by and between Registrant and NWALP PHOP Property Owner LLC.	10-Q	001-38276	7/31/2019	10.2	
10.21	Third Amendment to Lease, dated September 25, 2019, by and between Registrant and NWALP PHOP Property Owner LLC.	10-Q	001-38276	11/5/2019	10.1	
10.22	Equity Distribution Agreement, dated December 28, 2018, by and between the Registrant and Citigroup Capital Markets, Inc.	S-3	333-299091	12/28/2018	1.2	
10.23	Development Funding Agreement, dated as of February 28, 2019, by and between the Registrant and SFJ Pharmaceuticals XI, L.P.	10-Q	001-38276	5/7/2019	10.1	
10.24	Amendment, dated as of June 7, 2019, to the Development Funding Agreement, dated as of February 28, 2019 by and between the Registrant and SFJ Pharmaceuticals XI, L.P.	10-Q	001-38276	7/31/2019	10.1	
10.25	Standard Office Lease, dated as of March 29, 2019, by and between the Registrant and Geary-Market Investment Company, Ltd.	10-Q	001-38276	5/7/2019	10.2	
10.26	Offer Letter, dated as of April 13, 2018, by and between the Registrant and Lukas Scheibler	10-Q	001-38276	5/7/2019	10.3	
10.27	Form of Capped Call Transaction Confirmation	8-K	001-38276	9/16/2019	10.1	
10.28†	Apellis Pharmaceuticals, Inc. Executive Separation Benefits and Retention Plan	8-K	001-38276	10/7/2019	10.1	
21.1	Subsidiaries of the Registrant					X
23.1	Consent of Deloitte & Touche LLP					X
23.2	Consent of Ernst & Young LLP					X
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
32.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
32.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
101.INS	Inline XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document					
101.SCH	Inline XBRL Taxonomy Extension Schema Document					
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document					
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document					
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document					
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					

104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

* Pursuant to Item 601(b)(2) of Regulation S-K, the Registrant agrees to furnish supplementally a copy of any omitted schedule or exhibit to the Asset Purchase Agreement to the Securities and Exchange Commission upon request.

† Confidential treatment has been granted as to certain portions, which portions have been omitted and separately filed with the Securities and Exchange Commission.

+ Management contract or compensatory plan or arrangement.

Filed herewith.

Item 16. Form 10-K Summary.

Not applicable

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

Apellis Pharmaceuticals, Inc.

Date: February 27, 2020

By: /s/ Cedric Francois

Cedric Francois

President, Chief Executive Officer and Director

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Cedric Francois **Cedric Francois**	President, Chief Executive Officer and Director (Principal Executive Officer and Duly Authorized Officer)	February 27, 2020
/s/ Timothy E. Sullivan **Timothy E. Sullivan**	Chief Financial Officer and Treasurer (Principal Financial Officer and Duly Authorized Officer)	February 27, 2020
/s/ Nicole D. Perry **Nicole D. Perry**	Vice President, Finance (Principal Accounting Officer)	February 27, 2020
/s/ Gerald Chan **Gerald Chan**	Director	February 27, 2020
/s/ A. Sinclair Dunlop **A. Sinclair Dunlop**	Director	February 27, 2020
/s/ Alec Machiels **Alec Machiels**	Director	February 27, 2020
/s/ Stephanie M. O'Brien **Stephanie M. O'Brien**	Director	February 27, 2020

DESCRIPTION OF SECURITIES REGISTERED UNDER SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The following description of the common stock, par value $0.0001 per share (the "Common Stock"), of Apellis Pharmaceuticals, Inc. ("us," "our," "we" or the "Company"), which is the only security of the Company registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), summarizes certain information regarding the Common Stock in our restated certificate of incorporation, our amended and restated bylaws and applicable provisions of Delaware corporate law, and is qualified by reference to our restated certificate of incorporation and amended and restated bylaws, which are incorporated by reference as Exhibit 3.1 and Exhibit 3.2, respectively, to the Annual Report on Form 10-K.

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.

Common Stock

Voting Rights. Holders of our Common Stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders 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. Any matter other than the election of directors to be voted upon by the stockholders at such meeting will 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 when a different vote is required by law, our certificate of incorporation or our bylaws.

Dividends. Holders of Common Stock are entitled to receive proportionately any dividends as may be declared and paid on the Common Stock from funds lawfully available therefor as and when determined by our board of directors, subject to any preferential dividend rights of any outstanding preferred stock.

Liquidation and Dissolution. In the event of our liquidation or dissolution, whether voluntary or involuntary, 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.

Other Rights. 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. Outstanding shares of our Common Stock are non-assessable. Holders of our Common Stock are not, and will not be, subject to any liability as stockholders.

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws

Delaware law contains, 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 divide our board of directors into three classes with staggered three-year terms. In addition, a director may be removed only 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 be filled only 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 us.

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 amended and restated 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 amended and restated 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 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.

Issuance of Preferred Stock. Our board of directors is authorized, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series, and to fix the designations, powers, preferences and the relative, participating, optional or other special rights, and any qualifications, limitations and restrictions of the shares of each series of preferred stock. The issuance of preferred stock could impede the completion of a merger, tender offer or other takeover attempt.

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 us 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 amended and restated 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 shall be the sole and exclusive forum for (1) any derivative action or proceeding brought on behalf of the Company, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or stockholders to the Company or our stockholders, (3) any action asserting a claim against the Company 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 (4) any action asserting a claim against the 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.

Exhibit 21.1

SUBSIDIARIES OF APELLIS PHARMACEUTICALS, INC.

Subsidiary	Jurisdiction of Incorporation or Organization
Apellis Australia Pty Ltd.	Australia
Apellis Ireland Ltd.	Ireland
Apellis Switzerland GmbH	Switzerland
Apellis MA Securities Inc.	United States

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in Registration Statement No. 333-235830 and 333-229091 on Form S-3 and Registration Statement No. 333-229876 and 333-221528 on Form S-8 of our reports dated February 27, 2020, relating to the financial statements of Apellis Pharmaceuticals, Inc. and its subsidiaries and the effectiveness of Apellis Pharmaceuticals, Inc. and its subsidiaries' internal control over financial reporting appearing in the Annual Report on Form 10-K for the year ended December 31, 2019.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
February 27, 2020

Exhibit 23.2

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-3 No. 333-235830) of Apellis Pharmaceuticals, Inc., and
(2) Registration Statement (Form S-3 No. 333-229091) of Apellis Pharmaceuticals, Inc., and
(3) Registration Statement (Form S-8 No. 333-229876) pertaining to the 2017 Stock Incentive Plan, Inducement Stock Option Award, and 2017 Employee Stock Purchase Plan of Apellis Pharmaceuticals, Inc., and
(4) Registration Statement (Form S-8 No. 333-221528) pertaining to the 2010 Equity Incentive Plan, 2017 Stock Incentive Plan, and 2017 Employee Stock Purchase Plan of Apellis Pharmaceuticals, Inc.;

of our report dated February 26, 2019, with respect to the consolidated financial statements of Apellis Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) of Apellis Pharmaceuticals, Inc. for the year ended December 31, 2019.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 27, 2020

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Cedric Francois, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2019 of Apellis Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 27, 2020

By: /s/ Cedric Francois

Cedric Francois
Chief Executive Officer and President

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Timothy E. Sullivan, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2019 of Apellis Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 27, 2020

By: /s/ Timothy E. Sullivan

Timothy E. Sullivan
Chief Financial Officer and Treasurer

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Apellis Pharmaceuticals, Inc. (the "Company") on Form 10-K for the year ending December 31, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Cedric Francois, the Chief Executive Officer and President of the Company, hereby certifies, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that, to the best of his knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 27, 2020

By: /s/ Cedric Francois

Cedric Francois
Chief Executive Officer and President

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Apellis Pharmaceuticals, Inc. (the "Company") on Form 10-K for the year ending December 31, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Timothy Sullivan, Chief Financial Officer and Treasurer of the Company, hereby certifies, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that, to the best of his knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 27, 2020

By: /s/ Timothy E. Sullivan
Timothy E. Sullivan
Chief Financial Officer and Treasurer