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, 2021

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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒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, 2021, 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 $4,074,163,162. The number of shares of the registrant's common stock, par value $0.0001 per share outstanding as of February 23, 2022 was 97,731,353.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A in connection with its 2022 Annual Meeting of Stockholders within 120 days of the end of the registrant's fiscal year ended December 31, 2021. 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 Swedish Orphan Biovitrum AB (Publ) 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;
- the ongoing commercialization of EMPAVELI and our preparation for the commercialization of intravitreal pegcetacoplan;
- our sales, marketing and distribution capabilities and strategies, including for the commercialization and manufacturing of EMPAVELI, intravitreal pegcetacoplan and any future products;
- the rate and degree of market acceptance and clinical utility of EMPAVELI, intravitreal pegcetacoplan and any future products;
- our plans to develop our current and future product candidates for any additional indications;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- 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 we may develop and the inhibition of C3;
- our plans to research and develop any current and future product candidates we may develop;
- our current and any future collaborations for the development and commercialization of our current and future product candidates;
- the potential benefits of any collaboration;
- 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;
- the impact of the COVID-19 pandemic on our clinical trials, business and operations; and
- the impact of new government laws and regulations (including tax).

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

Note Regarding Certain References in this Annual Report on Form 10-K

Unless otherwise stated or the context indicates otherwise, all references herein to "Apellis," "Apellis Pharmaceuticals, Inc.," "we," "us," "our," "our company," "the Company" and similar references refer to Apellis Pharmaceuticals, Inc. and its wholly owned subsidiaries.

In addition, unless otherwise stated or the context indicates otherwise, all references in this Annual Report on Form 10-K to "EMPAVELI (pegcetacoplan)" and "EMPAVELI" refer to pegcetacoplan in the context of the commercially available product for which we received approval from the United States Food and Drug Administration in May 2021 for the treatment of adults with paroxysmal nocturnal hemoglobinuria, or PNH, and references to Aspaveli refer to pegcetacoplan in the context of the commercially available product for which Swedish Orphan Biovitrum AB (publ) and us received approval from the European Commission in December 2021 for the treatment of adults with PNH who are anemic after treatment with a C5 inhibitor for at least three months, in each case as more fully described herein; whereas, unless otherwise stated or the context indicates otherwise, all references herein to "pegcetacoplan" refer to pegcetacoplan in the context of the product candidate for which we are exploring further applications and indications, as more fully described herein. The other trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners.

RISK FACTOR SUMMARY

Our business is subject to a number of risks that if realized could materially affect our business, financial condition, results of operations, cash flows and access to liquidity. These risks are discussed more fully in the "Risk Factors" section of this Annual Report on Form 10-K. Our principal risks include the following:

- We have incurred significant losses since inception, we expect to incur losses for at least this year and next year, and we may never achieve or maintain profitability. Our net losses were $746.4 million, $344.9 million, and $304.7 million for the years ended December 31, 2021, 2020 and 2019, respectively. We have obtained marketing approval for EMPAVELI for the treatment of paroxysmal nocturnal hemoglobinuria, or PNH, and have neither obtained marketing approval for, nor commercialized, any other products for any other indications, which may make it difficult to evaluate our future prospects. We will need to continue to transition from a company with a development focus to a company capable of conducting successful commercial activities.
- Our long-term prospects depend upon the success of our intravitreal pegcetacoplan program, among other things. We plan to submit a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, in the second quarter of 2022 for the approval of intravitreal pegcetacoplan for the treatment of geographic atrophy, or GA, which submission would be supported by the completed Phase 2 and Phase 3 clinical trials of intravitreal pegcetacoplan in patients with GA. Any delay in submitting the NDA, or adverse action by the FDA, could delay our planned commercial development timelines or could prevent us from commercializing intravitreal pegcetacoplan. If the FDA determines that our NDA and the data supporting the NDA are not sufficient to support approval in GA, we may be required to conduct an additional clinical trial, which would increase our costs and delay the program. Any such delay or other adverse impact could have a material adverse effect on our business.
- We will need substantial additional funding to allow us to support both the systemic and intravitreal pegcetacoplan programs through commercial launch, and, if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate product development programs or commercialization efforts. We believe that our existing cash, cash equivalents and marketable securities, along with cash anticipated to be generated from sales of EMPAVELI, the $50.0 million first regulatory and reimbursement milestone payment, and the committed development reimbursement payments from Sobi, will enable us to fund our operating expenses and capital expenditure requirements at least into the second quarter of 2023.
- We are required to make substantial payments to SFJ Pharmaceuticals Group, or SFJ, pursuant to our development funding agreement as a result of receiving regulatory approval of EMPAVELI and Aspaveli in the United States and the European Union. 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.
- We are dependent on the successful commercialization of EMPAVELI in PNH and successful development and commercialization of pegcetacoplan in other disease indications. If we are unable to successfully commercialize EMPAVELI or develop and obtain marketing approval for or successfully commercialize pegcetacoplan in other indications, either alone or through a collaboration, or if we experience significant delays in doing so, our business could be harmed.

- The regulatory approval process is expensive, time consuming and uncertain and may prevent us or our collaborators such as Swedish Orphan Biovitrum AB (Publ), or Sobi, from obtaining marketing approvals for systemic pegcetacoplan in indications other than PNH or intravitreal pegcetacoplan for GA or other indications or any other product candidate that we develop in any jurisdiction. As a result, we cannot predict when or if, and in which jurisdictions, we, or our collaborators, will obtain marketing approval for systemic pegcetacoplan in other indications or intravitreal pegcetacoplan for GA or other indications or any other product candidate that we develop in any jurisdiction.
- The COVID-19 pandemic may affect our ability to initiate and complete preclinical studies and conduct our ongoing clinical trials, delay the initiation of planned and future clinical trials, disrupt regulatory activities, or have other adverse effects on our business and operations. In addition, the COVID-19 pandemic has adversely impacted economies worldwide, which could result in adverse effects on our business and operations.
- If clinical trials of systemic pegcetacoplan, intravitreal pegcetacoplan or our other product candidates fail to satisfactorily demonstrate safety and efficacy to the FDA, the European Medicines Agency, or EMA, and other regulators, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.
- We may not be able to switch patients who are being treated for PNH with eculizumab or ravulizumab, which are the current standard of care for PNH, to EMPAVELI, and EMPAVELI or any other product candidates that we develop 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 contract with third parties for the manufacture, storage and distribution of commercial and clinical supply of EMPAVELI and clinical supply for our product candidates and expect to continue to do so in connection with our development and commercialization efforts. This reliance on third parties increases the risk that we will not have sufficient quantities of EMPAVELI or our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts. If these third parties do not perform satisfactorily, our development or commercialization efforts could be delayed or impaired.
- Our prospects for the development and commercialization of systemic pegcetacoplan outside of the United States will depend in significant part on the success of our collaboration with Sobi.
- 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, including our patent license agreements with the University of Pennsylvania under which we license patents with claim that recite a class of compounds generically covering pegcetacoplan and APL-9, and that specifically recite the active component.

PART I

Item 1. Business.

We are a commercial-stage biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutic compounds to treat diseases with high unmet needs 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.

In May 2021, the U.S. Food and Drug Administration, or the FDA, approved EMPAVELI (systemic pegcetacoplan), the first targeted C3 therapy and our first approved product, for the treatment of paroxysmal nocturnal hemoglobinuria, or PNH. EMPAVELI is approved for use in adults with PNH and can be used by patients who are either treatment-naïve or who are switching from C5 inhibitors eculizumab or ravulizumab. We believe that EMPAVELI has the potential to elevate the standard of care in PNH and are seeking to establish EMPAVELI as the preferred first-line treatment for patients. In the United States, there are approximately 1,500 patients with PNH currently being treated with C5 inhibitors and another 150 patients who we estimate will be newly diagnosed each year. Between our launch of EMPAVELI in May 2021 through December 31, 2021, we generated $15.1 million in net product revenue from sales of EMPAVELI.

In December 2021, the European Commission, or the EC, approved Aspaveli (systemic pegcetacoplan) for the treatment of adults with PNH who are anemic after treatment with a C5 inhibitor for at least three months. In January 2022, systemic pegcetacoplan was also approved for the treatment of PNH in Saudi Arabia and Australia. Systemic pegcetacoplan is currently marketed under the trade name EMPAVELI™ in the United States, Saudi Arabia and Australia and Aspaveli® in the European Union. Under our collaboration and license agreement with Swedish Orphan Biovitrum AB (Publ), or Sobi. Sobi has global co-development and exclusive ex-U.S. commercialization rights for systemic pegcetacoplan and intends to initiate the commercial launch of Aspaveli in jurisdictions outside of the United States during the first quarter of 2022. We have commercialization rights for systemic pegcetacoplan in the United States.

We also are leveraging our expertise in targeting C3 to advance intravitreal pegcetacoplan as the first potential treatment for geographic atrophy, or GA, secondary to age-related macular degeneration, or AMD. Intravitreal pegcetacoplan has the potential to be a breakthrough for patients with GA, a disease that affects approximately one million people in the U.S. and five million people worldwide. Based on the results of our Phase 3 (DERBY and OAKS) and Phase 2 (FILLY) clinical trials of intravitreal pegcetacoplan, we intend to submit a new drug application, or NDA, to the FDA in the second quarter of 2022 with a request for six-month priority review. We also plan to submit a market authorization application, or MAA, to the European Medicines Agency, or the EMA, in the second half of 2022. We have exclusive, worldwide commercialization rights for intravitreal pegcetacoplan.

We believe that inhibition of the complement system by targeting C3 may enable a broad range of therapeutic approaches, and that pegcetacoplan has the potential to address the limitations of existing treatment options or provide a treatment option in indications where there currently are none. Under our collaboration with Sobi, we are co-developing systemic pegcetacoplan for cold agglutinin disease, or CAD, and hematopoietic stem cell transplantation-associated thrombotic microangiopathy, or HSCT-TMA, in hematology; C3 glomerulopathy, or C3G, and immune complex membranoproliferative glomerulonephritis, or IC-MPGN, in nephrology; and amyotrophic lateral sclerosis, or ALS, in neurology.

We are also evaluating the administration of systemic pegcetacoplan as an approach to enabling adeno-associated virus, or AAV, vector administration for gene therapies. Gene therapies delivered by AAVs have historically faced safety and tolerability challenges associated with potentially severe, or even fatal, side effects in patients. We believe complement inhibition may yield benefits when used in combination with AAV-delivered gene therapies. In collaboration with commercial and academic researchers, we are conducting pre-clinical studies to assess the impact of complement inhibition on AAV-delivered gene therapies and expect to report pre-clinical data in the first half of 2022.

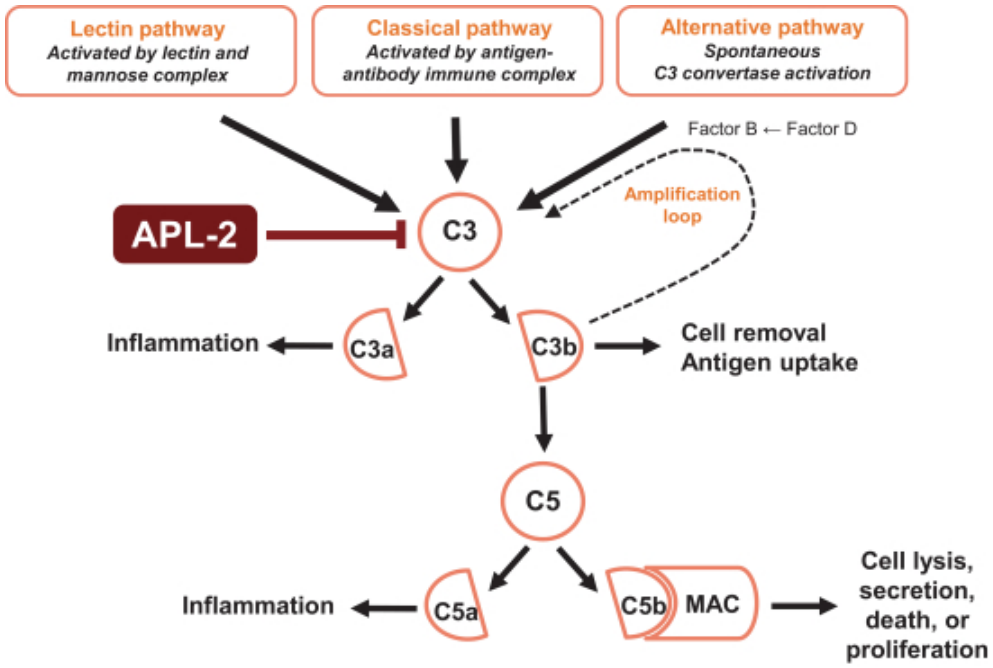
Lastly, we are developing other product candidates with other routes of administration and plan to conduct clinical trials of these product candidates, including the combination of EMPAVELI and a small interfering RNA, or siRNA, which may offer the potential to reduce the treatment frequency of EMPAVELI by reducing the production of C3 proteins in the liver. Furthermore, we are collaborating with Beam Therapeutics, Inc., or Beam, on six research programs focused on C3 and other complement targets in the eye, liver and brain, using Beam's proprietary base editing technology to discover new treatments for complement-driven diseases.

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, and others to depolarize or lose membrane potential.

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. 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.

Our Strategy

We aim to become a leading biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutic compounds to treat diseases in areas such as rare disease, ophthalmology and neurology through the inhibition of the complement system. We hold commercialization rights for systemic pegcetacoplan, which includes EMPAVELI, in the United States and worldwide commercialization rights to intravitreal pegcetacoplan, which includes our GA program, in addition to worldwide

commercialization rights for our other novel compounds targeting complement. To achieve our goals, we are pursuing the following strategies in 2022 with a continued focus on compassion and commitment to patients:

- ***Bringing intravitreal pegcetacoplan as the first-ever therapy to patients with GA***. We are developing intravitreal pegcetacoplan as monotherapy for GA. Based on the results of our Phase 3 and Phase 2 clinical trials, we are preparing submissions to regulatory authorities for marketing approval of intravitreal pegcetacoplan as a treatment for GA secondary to AMD. We intend to submit an NDA to the FDA in the second quarter of 2022 with a request for six-month priority review. We also plan to submit an MAA to the EMA in the second half of 2022.
- ***Further establishing EMPAVELI as a first-line treatment in PNH.*** Systemic pegcetacoplan, administered by subcutaneous injection, is commercially available as a monotherapy for adult patients with PNH in the United States. We are continuing our efforts to make EMPAVELI available to all adult U.S. patients with PNH, regardless of their baseline hemoglobin levels. We are also supporting Sobi's commercialization efforts of systemic pegcetacoplan for the treatment of PNH in the rest of the world.
- ***Evaluating systemic pegcetacoplan as a transformative therapy for rare, complement-driven diseases.*** We are evaluating systemic pegcetacoplan for patients with ALS and C3G/IC-MPGN, administered by subcutaneous injection. Sobi has primary responsibility for the clinical development of systemic pegcetacoplan for patients with CAD and HSCT-TMA.
- ***Advancing systemic pegcetacoplan as a novel approach to enabling AAV-delivered gene therapies***. We are advancing systemic pegcetacoplan as a novel approach to enabling AAV vector administration for gene therapies.
- ***Expanding clinical pipeline with new programs to control complement***. We plan to continue the development of treatments for a broad range of complement-dependent autoimmune and inflammatory diseases with pegcetacoplan, APL-2006, APL-1030 and our siRNA + EMPAVELI combination, as well as new product candidates and research activities under collaboration with Beam to develop gene-editing therapies in multiple therapeutic areas.

Our Programs

Pegcetacoplan targets C3, the central protein of the complement cascade. 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 have developed and are developing pegcetacoplan and other product candidates through various routes of administration.

The following table summarizes key information about our clinical programs:

Program	Clinical Trials	Trial Participants	Timeline
		Intravitreal pegcetacoplan	
GA	Phase 3 trials (DERBY/OAKS)	Patients with GA	NDA submission expected 2Q 2022
	Phase 2 trial (FILLY)	Patients with GA	Data reported in Aug 2017
		Systemic pegcetacoplan	
PNH	Phase 3 trial (PEGASUS)	Eculizumab-treated patients with PNH	Approved in May 2021
	Phase 3 trial (PRINCE)	Treatment-naïve patients with PNH	
C3G/IC-MPGN	Phase 3 Trial (VALIANT)	Patients with native kidney or post-transplant recurrence of C3G or IC-MPGN	Initiation expected 1H 2022
	Phase 2 trial (DISCOVERY)	Patients with glomerular diseases with complement involvement	Data reported in Oct 2020
	Phase 2 Trial (NOBLE)	Patients with post-transplant recurrence of C3G or IC-MPGN	First patient treated in Sept 2021
ALS	Phase 2 Trial (MERIDIAN)	Patients with sporadic ALS	Expected enrollment completion in 1H 2022
CAD	Phase 3 Trial	Patients with CAD	Initiation expected 1H 2022 (Sobi)
	Phase 2 Trial (PLAUDIT)	Patients with CAD and wAIHA	Data reported Jun 2019
HSCT-TMA	Phase 2 Trial	Patients with HSCT-TMA	First patient treated early 2022 (Sobi)
		Pipeline	

APL-1030	Preclinical	Undisclosed	IND expected 2H 2022
APL-2006	Preclinical	GA & Wet AMD	IND expected 1H 2023
EMPAVELI+ siRNA	Preclinical	Existing + new indications	IND expected 1H 2023

Ophthalmology

We are developing intravitreally delivered pegcetacoplan as a monotherapy for patients with GA.

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 estimate that at least five million people worldwide, including at least one million people in the United States, are living with GA.

At the American Academy of Ophthalmology, or AAO, in November 2020, a retrospective study of 69,000 patients diagnosed with GA was presented that analyzed changes in visual acuity and disease progression over two years. The analysis was presented by Verana Health, a data analysis group in retinal diseases under a collaboration with us, and the AAO's IRIS (Intelligent Research in Sight) Registry, the nation's first comprehensive clinical registry for eye disease. Key findings from the real-world clinical data showed:

- At the first study visit, patients presented with relatively preserved vision, especially in eyes with extrafoveal GA lesions (lesions outside the fovea, which is the central portion of the retina). However, patients with extrafoveal and foveal GA lesions progressively lost vision over time at a rate of approximately five letters on a vision chart per year.
- Progression from GA to new onset wet AMD was observed in 4.7% of patients with bilateral GA (GA in both eyes) and 13.3% of patients with wet AMD in the contralateral eye (AMD in the non-treatment eye) during the first 12 months. The rate at 24 months was 8.2% and 21.6% in bilateral GA and wet AMD in the contralateral eye, respectively.
- A large proportion of GA patients did not return for a follow-up visit after two years. Of the GA patients potentially eligible for inclusion in the analysis, only 40% had a follow-up visit after two years and were ultimately included in the study.

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 it 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 including a number of product candidates in mid- to late stages of clinical development.

Benefits of Our Approach

We believe intravitreal 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 intravitreal pegcetacoplan may mitigate or prevent retinal cell death in GA, leading to a reduction in GA lesion growth over time. In our Phase 3 DERBY and

OAKS trials and our Phase 2 FILLY trial, pegcetacoplan showed what we believe to be a clinically meaningful reduction of GA lesion growth in both monthly and every-other-month dosing, with a favorable safety profile.

- *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 and Phase 3 trials, that the activity of pegcetacoplan does not depend upon the activation of any particular complement pathway.

Clinical Development

We initiated the Phase 3 DERBY and OAKS trials evaluating the efficacy and safety of intravitreal pegcetacoplan in patients with GA secondary to AMD in September 2018. In September 2021, we reported top-line results from our DERBY and OAKS trials, followed by additional analyses presented at multiple medical meetings in October and November of 2021. In July 2018, we received fast track designation from the FDA for pegcetacoplan in GA. 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 post-treatment monitoring period from that trial. Prior to the FILLY trial, we completed a Phase 1 trial of pegcetacoplan in patients with wet AMD in 2016.

Phase 3 Clinical Trials

Our ongoing Phase 3 clinical program in GA consists of two prospective, multicenter, randomized, double-masked, sham-injection controlled trials (DERBY and OAKS) being conducted at 200 sites worldwide to assess the efficacy and safety of multiple intravitreal injections of pegcetacoplan in patients with GA. We enrolled 621 patients in DERBY and 637 patients in OAKS.

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 FILLY clinical trial, the primary endpoint of each trial was 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 was analyzed at 12 months (primary endpoint, monthly group) and will be analyzed at 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 continued to be treated with pegcetacoplan along with anti-VEGF injections, the current standard of care for wet AMD.

We completed the primary endpoint analysis for the 12-month treatment period in September 2021. Monthly and every-other-month treatment with intravitreal pegcetacoplan met the primary endpoint in OAKS, significantly reducing GA lesion growth by 22% (p=0.0003) and 16% (p=0.0052), respectively, compared to pooled sham at 12 months. Monthly and every-other-month treatment with pegcetacoplan did not meet the primary endpoint in DERBY, showing a reduction in GA lesion growth of 12% (p=0.0528) and 11% (p=0.0750), respectively, compared to pooled sham at 12 months. In a prespecified analysis of the combined DERBY and OAKS studies, monthly and every-other-month treatment with pegcetacoplan reduced GA lesion growth by 17% (p<0.0001) and 14% (p=0.0012), respectively, compared to pooled sham at 12 months.

In a prespecified analysis of the primary endpoint, pegcetacoplan demonstrated a greater effect in patients with extrafoveal lesions at baseline. Patients with GA typically present first with extrafoveal lesions, which then progress toward the fovea where central vision is impacted. Under the prespecified analysis, in the combined studies, monthly and every-other-month treatment with pegcetacoplan decreased GA lesion growth by 26% (p<0.0001) and 23% (p=0.0002), respectively, in patients with extrafoveal lesions compared to pooled sham at 12 months.

Intravitreal pegcetacoplan was well-tolerated in both DERBY and OAKS. The pooled rate of new-onset exudations was 6.0% of patients in the monthly treatment groups, 4.1% in the every-other-month treatment groups, and 2.4% in the sham groups. Consistent with our Phase 2 FILLY trial, we defined and reported exudations as all adverse events of exudative AMD that were reported by the investigator, regardless of whether there was confirmation from the reading center. Two cases of confirmed infectious endophthalmitis and one case of suspected infectious endophthalmitis were observed in the study eye out of a total of 6,322 injections (0.047%). Rates of endophthalmitis and intraocular inflammation were generally in line with those reported in studies of other intravitreal therapies. Fourteen events of intraocular inflammation, including one event of non-infectious endophthalmitis, were observed in the studies (0.22% per injection). No events of retinal vasculitis or retinal vein occlusion were observed. There were no clinically relevant changes in vision for patients who developed infectious endophthalmitis or intraocular inflammation.

We expect to report additional 18-month safety and efficacy data in March 2022 and 24-month data, including the functional secondary endpoints, during the third quarter of 2022.

We plan to submit an NDA to the FDA in the second quarter of 2022 with a request for six-month priority review, based on the results from DERBY, OAKS and FILLY, and the feedback from the FDA on our regulatory strategy. We completed a pre-NDA meeting with the FDA in January 2022. We plan to begin pre-submission disclosures to the EMA in the first quarter of 2022 andto submit an MAA to the EMA in the second half of 2022.

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 FILLY, our Phase 2 multicenter, randomized, single-masked, sham-controlled clinical trial of intravitreal pegcetacoplan in patients with GA, at more than 40 clinical sites primarily located in the United States. We enrolled 246 patients in the trial. Patients were randomized in a 2:2:1:1 manner to receive 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 received 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.

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 Clinical Trial in Low Vision Geography Atrophy

In September 2018, we initiated a Phase 1b clinical trial to evaluate the safety of monthly intravitreal treatments with pegcetacoplan in 12 patients with bilateral GA secondary to AMD and with low vision. Patients were dosed monthly with pegcetacoplan in one eye using the fellow eye as an untreated control. In April 2020, we reported results in patients demonstrating a trend in reduced GA lesion growth in treated eyes versus the lesion growth in untreated fellow eyes. In October 2020, we reported data from an 18-month post hoc analysis based on the seven study patients for whom data were available for at least 18 months. In this population, the growth rate of GA lesions in the treated eye was on average 52% (mean square root) slower than the untreated fellow eye (p=0.01). Of the 12 enrolled patients, there were no reported cases of inflammation and one patient (8%) developed new-onset exudation at month 12.

Phase 1b/2 Clinical Trial in Wet AMD

In the second quarter of 2018, 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. 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 discontinued the Phase 1b/2 trial of pegcetacoplan in patients with wet AMD.

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 pharmacokinetics of pegcetacoplan. In this trial, patients received a single dose of pegcetacoplan by intravitreal injection followed by 113 days of monitoring. We enrolled 18 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.

Preclinical Studies

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

Intermediate AMD (iAMD)

Based on feedback from the FDA, we believe that pivotal studies in iAMD would involve a large number of patients over an extended period of time, and therefore, we have decided to deprioritize our development program in iAMD for now. This decision does not minimize our view of the unmet need in this disease or the benefit of pegcetacoplan as a potential treatment.

GA + Wet AMD

We plan to submit an IND application for APL-2006, a bispecific C3 and VEGF inhibitor, in the first half of 2023. There are currently a high proportion of patients who are currently living with advanced forms of AMD, including both GA and wet AMD, and we believe APL-2006 has the potential to benefit these patients.

We have exclusive, worldwide rights for the development and commercialization of intravitreal pegcetacoplan and for APL-2006.

Rare Disease

Together with Sobi, we are developing systemic pegcetacoplan in multiple late-stage programs in rare disease indications across hematology, nephrology, and neurology. We are leading the clinical development for the treatment of C3G/IC-MPGN and ALS, and Sobi is leading the clinical development for the treatment of CAD and HSCT-TMA. In PNH, we and Sobi have now obtained approval of systemic pegcetacoplan in multiple jurisdictions, including the United States and the European Union.

Paroxysmal Nocturnal Hemoglobinuria (PNH)

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 and approximately 15,000 patients with PNH worldwide.

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 and ravulizumab are C5 inhibitors marketed by AstraZeneca Rare Disease, or AstraZeneca, and were the only therapies approved for the treatment of PNH prior to the approval of EMPAVELI. 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 week 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 eculizumab and was found to be non-inferior to eculizumab.

Retrospective third-party 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 continuing 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 systemic pegcetacoplan inhibits complement activation at the level of C3, and based on the results from our Phase 3 PEGASUS and PRINCE studies, systemic pegcetacoplan provides the following benefits in controlling PNH:

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

Regulatory Matters

We submitted an NDA to the FDA and an MAA to the EMA for systemic pegcetacoplan for the treatment of PNH in September 2020. In May 2021, systemic pegcetacoplan was approved by the FDA with the brand name EMPAVELI for the treatment of adult patients with PNH. In December 2021, the EC approved systemic pegcetacoplan with the brand name Aspaveli for the treatment of adults with PNH who are anemic after treatment with a C5 inhibitor for at least three months. In January 2022, pegcetacoplan was also approved as EMPAVELI in Saudi Arabia and Australia. Under our agreement with Sobi, we are eligible for a $50.0 million milestone

payment from Sobi upon first European regulatory approval, which was obtained in December 2021, and reimbursement approval, which has not yet been obtained. We expect to receive this milestone payment from Sobi in the first half of 2022.

Clinical Development

We believe that systemic pegcetacoplan is a best-in-class therapy for PNH, differentiated by mechanism, and that it has the potential to significantly increase the quality of life of patients with PNH as compared to the current standard of care.

Phase 3 Clinical Trial - PEGASUS

We initiated the Phase 3 PEGASUS trial in patients in June 2018. The PEGASUS trial was an 80-patient randomized head-to-head trial comparing systemic 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 was the change in hemoglobin level from baseline at week 16.

The treatment period of the trial consisted 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 received 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 systemic 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.

All patients who completed the 16-week randomization period in both groups (77/80) entered the 32-week open-label pegcetacoplan treatment period. At week 48, patients treated with pegcetacoplan during the 16-week randomization period and through the 32-week open-label period sustained increases in hemoglobin levels, with a mean improvement from baseline of 2.7 g/dL, equal to the 2.7 g/dL mean increase seen at week 16 in the same patients. Additionally, patients treated with eculizumab in the randomized period who switched to pegcetacoplan during the open-label period experienced sustained improvements in hemoglobin and other hematological and clinical measures, similar to patients treated with pegcetacoplan monotherapy during the randomized controlled period. In addition to a sustained improvement in hemoglobin, the pegcetacoplan-treated patients group maintained improvements across key secondary endpoints. Throughout the 48-week study, 73% of patients treated with pegcetacoplan during the randomized period remained transfusion free. For comparison, 25% of patients were transfusion free over the year prior to entering the PEGASUS study while on treatment with eculizumab. Improvements across additional markers of disease, such as reticulocyte count, lactate dehydrogenase, or LDH, levels, and the FACIT-fatigue scores, were observed in both groups at week 48 after 32 weeks of open-label treatment with pegcetacoplan.

In the PEGASUS trial, the safety profile of systemic pegcetacoplan was comparable to eculizumab and consistent with previously reported data. After the 48-week study period, twenty-four of 80 pegcetacoplan monotherapy-treated patients (30%) experienced a serious adverse event (SAE). Five of the SAEs (6%) were assessed to be possibly related to study treatment. No cases of meningitis were reported. One death was reported due to COVID-19 and was unrelated to study treatment. The most common adverse events (AEs) reported throughout the study were injection site reactions (36%), hemolysis (24%), and diarrhea (21%). Twelve out of 80 patients (15%) discontinued due to adverse events, with five discontinuations due to hemolysis. Sixty-four of the 67 patients (96%) who completed the open-label period opted to enter the extension study.

Phase 3 Clinical Trial – PRINCE

We initiated the Phase 3 PRINCE trial in September 2019. The PRINCE trial was a 54-patient randomized, multicenter, open-label trial to evaluate the efficacy of systemic pegcetacoplan in treatment-naïve PNH patients. The primary endpoints were 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 LDH level from baseline to week 26, in patients with PNH who are currently not being treated with complement inhibitors. Secondary endpoints included 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.

In May 2021, we reported top-line results from PRINCE demonstrating statistical superiority on the co-primary endpoints of hemoglobin stabilization and reduction in LDH compared to standard of care, which did not include complement inhibitors, at week 26. Specifically, 86% of EMPAVELI-treated patients achieved hemoglobin stabilization compared to 0% of patients on standard of care ($p<0.0001$). Hemoglobin stabilization was defined as an avoidance of a >1 g/dL decrease in hemoglobin levels in the absence of transfusions. Additionally, mean LDH in the EMPAVELI group decreased by 90% from a baseline of 2151 U/L, which is 9.5 times the upper limit of normal (ULN), to 211 U/L, which is within the normal range, compared to a 14% reduction on standard of care from a baseline of 1946 U/L to 1681 U/L ($p<0.0001$).

EMPAVELI also achieved statistical superiority on several secondary endpoints, including improvements in hemoglobin levels and transfusion avoidance, compared to standard of care, which did not include complement inhibitors. Mean hemoglobin levels in the EMPAVELI group increased from 9.4 g/dL to 12.1 g/dL compared to an increase from a baseline of 8.7 g/dL to 9.4 g/dL on standard of care ($p=0.0019$). Further, 91% of patients on EMPAVELI avoided transfusions compared to 6% on standard of care ($p<0.0001$).

Phase 1b Clinical Trials – PHAROAH and PADDOCK

Prior to commencing our two Phase 3 trials, we conducted two clinical trials of systemic 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 a Phase 1b clinical trial (PADDOCK) in treatment-naïve patients. 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 systemic 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 was a Phase 1b open-label clinical trial of systemic pegcetacoplan in treatment-naïve patients with PNH that we initiated in December 2015 and conducted 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 treated a total of 22 patients in the PADDOCK trial. 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.

Long-Term Extension Study

We are conducting a long-term extension study of systemic 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. 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 patients with PNH is terminated.

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

We have completed both a single ascending and multiple ascending dose Phase 1 randomized, double-blind, placebo-controlled clinical trials of systemic pegcetacoplan in a total of 55 healthy volunteers. We conducted the trials at a single site in Australia to assess the safety, tolerability, pharmacokinetics, or 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 systemic pegcetacoplan in patients with renal impairment. The study included 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 evaluated 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 established the dosing regimen in PEGASUS and PRINCE based on this trial.

We conducted a Phase 1 trial to determine the safety, PK and PD of pegcetacoplan in healthy volunteers of Japanese descent. We evaluated whether pegcetacoplan will have comparable PK and PD profiles in this population. No significant difference in PK parameters was noted.

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.

Through January 2022, systemic pegcetacoplan has been administered to 313 subjects with approximately 420 patient-years of exposure in the clinical trial setting, and, since commercial launch in May 2021, to approximately 120 patients with approximately 50 patient-years of exposure in the post-marketing setting. No unexpected safety concerns have been observed in any of these patients.

Small interfering RNA, or siRNA + EMPAVELI

We plan to submit an IND for the combination of EMPAVELI and a small interfering RNA, or siRNA, in the first half of 2023. This combination may offer the potential to reduce the treatment frequency of EMPAVELI by reducing the production of C3 proteins by the liver.

Commercial and Medical Activities for PNH Launch

We launched EMPAVELI in the United States for patients with PNH following its approval by the FDA in May 2021. We believe that with EMPAVELI we can elevate the standard of care for patients and are seeking to further establish EMPAVELI as first-line treatment. We have demonstrated strong progress to date. Between launch through December 31, 2021, we generated net product revenue of $15.1 million.

Our sales team is covering the health care professionals, or HCPs, and key treatment centers, focusing on HCPs who have patients that continue to experience breakthrough hemolysis, have persistently low hemoglobin, high fatigue, and require transfusions despite being on C5 inhibitors. The team is engaging both in-person and virtually with HCPs, closely monitoring regional COVID-19 restrictions and pursuing in-person engagements when able to and in compliance with appropriate guidelines.

Our market access team is engaging with primary and secondary payers representing a significant percentage of PNH patients. Our discussions with primary and secondary payers have yielded positive feedback on the clinical profile of pegcetacoplan and resulted in EMPAVELI being added to several positive formulary positions. We implemented a limited distribution specialty pharmacy model, which we believe provided patients with a consistent, positive experience at the time of treatment initiation and long-term assistance to the extent needed.

We also established Apellis Assist, a patient-focused program specifically designed to assist patients with onboarding, product training and ongoing support with pegcetacoplan treatment, and have built a care educator team to connect directly with PNH patients and their caregivers to provide education and training on the use of pegcetacoplan.

We are developing ENABLE, 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 are using one or more commercially available ambulatory infusion pumps for commercial use of pegcetacoplan as a treatment for PNH.

Our medical affairs team is engaging with physicians, either in-person or virtually, and through our presence at medical meetings and other in-person engagements when appropriate. In December 2021, we participated in the American Hematology Society, or ASH, annual meeting. We will continue to leverage this platform for future medical congresses. We have initiated an early access program and have already established multiple U.S. sites for patients. Sobi will conduct medical affairs activities for systemic pegcetacoplan outside the United States.

C3 Glomerulopathy (C3G) and Immune Complex Membranoproliferative Glomerulonephritis (IC-MPGN)

C3G and IC-MPGN are rare, debilitating kidney diseases that affect approximately 18,000 people in the United States and Europe. There are no approved therapies for the diseases, and symptoms include blood in the urine, dark foamy urine due to the presence of protein, swelling, and high blood pressure. Approximately 50% of people living with C3G and IC-MPGN ultimately suffer kidney failure within five to 10 years of diagnosis. Although IC-MPGN is considered a distinct disease from C3G, the underlying cause and progression of the two diseases are remarkably similar and include overactivation of the complement cascade, with excessive accumulation of C3 breakdown products in the kidney causing inflammation and damage to the organ. There are no medicines currently approved for C3G or IC-MPGN. 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 December 2018, systemic pegcetacoplan received orphan drug designation from the FDA for the treatment of C3G.

In February 2018, we initiated DISCOVERY, a Phase 2 clinical trial of systemic 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. Initially each patient received once daily subcutaneous infusions of up to 360 mg of pegcetacoplan for one year, but patients could elect to receive twice weekly subcutaneous infusions of 1080 mg after week 24. The primary efficacy endpoint was the reduction in proteinuria, an important market of kidney damage, from baseline to week 48 as quantified by protein-to-creatinine ratio, or 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 included analysis of serum C3 and estimated glomerular filtration rate.

In October 2020, we reported data from the DISCOVERY trial in five C3G patients treated with systemic pegcetacoplan for 48 weeks. In those patients, mean (SE) proteinuria decreased from 3.48 (0.82) mg/mg at baseline to 0.93 (0.27) mg/mg at week 48, a decrease of 73.3%, as measured by 24-hour uPCR. Importantly, this reduction in proteinuria was accompanied by a corresponding increase in mean serum albumin. Since albumin is the most abundant protein in serum, its level increases when urinary protein losses are reduced. Other biomarkers improved, including an observed increase in mean serum C3 and stabilization of renal function, as measured by mean serum creatinine. No serious or severe adverse events were reported, and pegcetacoplan was well tolerated overall.

In September 2021, we initiated our registrational program in C3G and IC-MPGN with our NOBLE trial, a randomized, controlled Phase 2 trial in 12 patients with post-transplant disease recurrence that focused on the histopathology of the kidneys. Trial participants are randomized in a 3:1 ratio to receive pegcetacoplan or maintain standard of care for 12 weeks and then all patients in the study will receive pegcetacoplan from week 13 to week 52. The primary endpoint of the study is the proportion of patients with reduction in C3c staining on renal biopsy after 12 weeks of treatment with pegcetacoplan. Secondary endpoints include an evaluation of safety, the proportion of patients with reduction in C3c staining on renal biopsy after 52 weeks of treatment, and the proportion of patients achieving at least a 50% reduction in proteinuria.

We expect to dose our first patient in our Phase 3 VALIANT trial in the first half of 2022. VALIANT is a randomized, placebo-controlled, double-blinded, multi-center Phase 3 trial being conducted in approximately 90 patients who are 12 years of age and older with primary IC-MPGN or C3G. VALIANT is the only study to include both native kidney patients and patients who have recurrent disease after receiving a kidney transplant.

Cold Agglutinin Disease (CAD)

CAD is a severe, chronic, rare blood disorder that impacts about 10,500 people across the United States and Europe. People living with CAD may suffer from chronic anemia, transfusion requirements, and an increased risk of life-threatening thrombotic

events such as stroke. In people with CAD, immunoglobin M (IgM) autoantibodies cause red blood cells to agglutinate, or clump together, at temperatures below 30ºC or as a result of a compromised immune system or infection This activates the complement cascade to destroy healthy red blood cells through extravascular and intravascular hemolysis. In February 2022, the FDA granted approval for sutimlimab-jome, which was developed by Sanofi as a treatment for patients with 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. Sobi expects to dose the first patient in its Phase 3 trial in the first half of 2022.

In February 2022, the FDA granted approval for sutimlimab-jome to decease the need for red blood cell transfusions due to hemolysis in adults with CAD. Sutimlimab-jome was developed by Sanofi as a treatment for patients with CAD. Other 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.

In March 2018, we initiated PLAUDIT, our Phase 2 open label clinical trial of systemic pegcetacoplan administered by subcutaneous injection in patients with CAD. In the PLAUDIT trial, doses of pegcetacoplan were initially administered by subcutaneous injection during the treatment period, followed by a long-term extension period. 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)

Systemic pegcetacoplan was generally well tolerated in these patients in the PLAUDIT trial, with a safety profile similar to that of other studies of systemic administration of pegcetacoplan.

Hematopoietic Stem Cell Transplantation Thrombotic Microangiopathy

Hematopoietic stem cell transplantation thrombotic microangiopathy, or HSCT-TMA, is rare blood disease that can be a fatal complication of a bone marrow transplant or HSCT. In HSCT-TMA, microscopic blood clots form in small blood vessels, leading to organ damage. The kidneys are commonly affected, although any organ may be involved. HSCT-TMA occurs in up to 40% of HSCT recipients; every year, there are approximately 9,000 allogeneic transplants in the United States and approximately 18,000 in the European Union. Excessive complement activation is a high-risk feature in patients with HSCT-TMA, and C3 is believed to play a critical role in TMA based on proinflammatory and procoagulant properties of C3a and C3b.

In early 2022, Sobi dosed the first patient in the Phase 2 clinical trial of systemic pegcetacoplan in patients with HSCT-TMA.

Neurology

Amyotrophic Lateral Sclerosis (ALS)

We are also developing systemic pegcetacoplan for the treatment of ALS.

ALS is a devastating neurodegenerative disease that results in progressive muscle weakness and paralysis due to the death of nerve cells, called motor neurons, in the brain and spinal cord. The death of motor neurons leads to the progressive loss of voluntary muscle movement required for speaking, walking, swallowing, and breathing. In individuals with ALS, high levels of C3 are present at the neuromuscular junction where motor neurons communicate directly to muscle cells. Numerous studies suggest that elevated levels of C3 present throughout the motor system of ALS patients are likely to contribute to chronic neuroinflammation and the

death of motor neurons. There are currently no approved treatments that stop or reverse the progression of ALS, which impacts approximately 225,000 patients worldwide.

In November 2020, we dosed our first patient in MERIDIAN, a randomized, double-blind, placebo-controlled, multicenter Phase 2 clinical trial designed to evaluate the efficacy and safety of systemic pegcetacoplan in approximately 200 adults with sporadic ALS. Trial participants are randomized in a 2:1 ratio to receive pegcetacoplan or placebo while continuing to receive their existing standard of care treatment for ALS. After 52 weeks of blinded treatment, all patients in the study will receive pegcetacoplan. To reduce the burden on people living with ALS and their caregivers, the study has been designed to minimize the number of in-clinic visits, with approximately six clinic visits in the first year and four in the open-label second year. The primary endpoint of this trial is the Combined Assessment of Function and Survival (CAFS) rank scores at week 52. We expect to complete enrollment in MERIDIAN in the first half of 2022.

Neurodegenerative Diseases

Additionally, we are developing APL-1030, a novel, first-in-class C3 inhibitor designed to be administered to the brain intrathecally with the potential to treat multiple neurodegenerative diseases. We intend to submit an IND for APL-1030 in the second half of 2022.

Other Research

On June 30, 2021, we entered into an exclusive five-year research collaboration with Beam focused on the use of Beam's proprietary base editing technology to discover new treatments for complement-driven diseases. Under the collaboration agreement, we are collaborating on up to six research programs focused on C3 and other complement targets in the eye, liver and brain.

In March 2021, we announced that we will no longer pursue additional development of APL-9 for the treatment of severe COVID-19.

Collaboration and License Agreement with Sobi

In October 2020, we entered into a Collaboration and License Agreement with Sobi concerning the development and commercialization of pegcetacoplan and specified other compstatin analogues or derivatives for use systemically or for local non-ophthalmic administration, or Licensed Products. The agreement does not cover pegcetacoplan or other compstatin analogues or derivatives used for non-systemic ophthalmic administration or APL-9.

Under the agreement, we granted Sobi an exclusive (subject to certain rights retained by us), sublicensable license under certain patent rights and know-how to develop and commercialize Licensed Products in all countries outside of the United States.

We retained the right to commercialize Licensed Products in the United States, and, subject to specified limitations, to develop Licensed Products worldwide for commercialization in the United States.

Under the agreement, we and Sobi have agreed to collaborate to develop Licensed Products for the treatment of PNH, CAD, HSCT-TMA, C3G, IC-MPGN and ALS, or the "Initial Indications", and any other indications subsequently agreed upon by the parties, for commercialization by or on our behalf in the United States and by or on behalf of Sobi outside of the United States. If the parties do not agree to jointly pursue any development activities for the Licensed Products (whether for an Initial Indication or otherwise), the party proposing to pursue such activities may conduct such activities at its sole expense (with the non-proposing party having the right to obtain rights to the data generated by such development activities by paying a specified percentage of that expense), subject to agreed-upon exceptions that limit each party's unilateral development rights.

The initial development plan sets forth the initial development activities to be conducted by each of us and Sobi, with us bearing all costs incurred in conducting the activities set forth in such initial development plan, as well as certain specified additional costs that are not included in the initial development plan that may be incurred by the parties in developing Licensed Products for PNH in the European Union and the United Kingdom.

Each party is obligated to use commercially reasonable efforts to complete the development obligations assigned to it in the development plan. We are obligated to use commercially reasonable efforts to obtain regulatory approval from the FDA for a Licensed Product in each of the Initial Indications, to obtain regulatory approval from the EMA for a Licensed Product in PNH and to assist Sobi to obtain other regulatory and reimbursement approvals for Licensed Products outside of the United States. Sobi is obligated to use commercially reasonable efforts to develop and obtain regulatory approval for, and to commercialize, Licensed Products for each of the Initial Indications in specified major markets.

We have agreed to supply Sobi with Licensed Products for development and for commercialization outside of the United States in accordance with a supply agreement between the parties. Sobi has the right to perform or have performed drug product manufacturing of Licensed Products for development and for commercialization outside the United States and to manufacture or have manufactured drug substance under certain circumstances.

Together with Sobi, we have formed several governance committees to oversee the development and manufacture, and to review and discuss the commercialization, of Licensed Products.

We have agreed not to, directly or indirectly, alone or with or for any other person or entity, conduct any clinical development or commercialization of APL-9 for any Initial Indication or any other indications subsequently agreed upon by the parties.

Under the terms of the agreement, Sobi paid an upfront payment of $250.0 million, and agreed to pay us up to an aggregate of $915.0 million upon the achievement of specified one-time regulatory and commercial milestone events, including a $50.0 million milestone payment which would be payable upon the first regulatory and reimbursement approval for systemic pegcetacoplan in any major European country. Sobi also agreed to reimburse us for up to $80.0 million in development costs, of which we have received cash payments of $25.0 million to date. We will also be entitled to receive tiered, double-digit royalties (ranging from high teens to high twenties) on sales of Licensed Products outside of the United States, subject to customary deductions and third-party payment obligations, until the latest to occur of: (i) expiration of the last-to-expire of specified licensed patent rights; (ii) expiration of regulatory exclusivity; and (iii) ten (10) years after the first commercial sale of the applicable Licensed Product, in each case on a Licensed Product-by-Licensed Product and country-by-country basis. Under the agreement, we remain responsible for its license fee obligations (including royalty obligations) to the Penn and for our payment obligations to SFJ.

Unless earlier terminated, the agreement will expire upon the expiration of the last royalty term for the last Licensed Product outside of the United States. The agreement may be terminated in its entirety by Sobi upon 90 days' prior written notice at any time after the earlier of (i) October 27, 2022 or (ii) receipt of the first regulatory approval for the first Licensed Product in any of France, Germany, Italy, Spain, or the United Kingdom. Either party may, subject to specified cure periods, terminate the agreement in its entirety in the event of the other party's uncured material breach. In addition, we may, subject to specified cure periods, terminate the agreement in any of China, Japan, Brazil, or Canada if Sobi materially breaches its obligation to use commercially reasonable efforts to develop, obtain regulatory approval for, and commercialize a Licensed Product for PNH and ALS in such country. Either party may also terminate the agreement under specified circumstances relating to the other party's insolvency. We may terminate the agreement in the event Sobi or its specified affiliates or sublicensees challenges the validity, scope or enforceability of the licensed patent rights under specified circumstances.

Research Collaboration with Beam

On June 30, 2021, we entered into an exclusive five-year research collaboration with Beam focused on the use of Beam's proprietary base editing technology to discover new treatments for complement-driven diseases. Under the collaboration agreement, we are collaborating on up to six research programs focused on C3 and other complement targets in the eye, liver and brain.

Under the terms of the collaboration agreement, Beam will apply its base editing technology and conduct preclinical research on up to six base editing programs that target specific genes within the complement system in various organs including the eye, liver and brain. We have exclusive rights to license each of the six programs and will assume responsibility for subsequent development. Beam may elect to enter a 50-50 U.S. co-development and co-commercialization agreement with us with respect to any one program licensed under the collaboration.

As part of the collaboration, we paid Beam $50.0 million upon signing and are obligated to pay Beam an additional $25.0 million payment on June 30, 2022. After exercise of the opt-in license rights for each of the up to six programs, Beam will be eligible to receive development, regulatory and sales milestones from us, as well as royalty payments on sales. The collaboration has an initial term of five years and may be extended up to two years on a per year and program-by-program basis.

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.

As of December 31, 2021, we own a total of 17 U.S. patents, 26 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.

Pegcetacoplan and APL-9 are analogs of the cyclic peptide compstatin, based on technologies that we have developed internally or have exclusively licensed from the Trustees of the University of Pennsylvania, or Penn.

Our patents and patent applications include families of United States and foreign patent and patent applications relating, for example, to the composition of matter of 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. We have submitted applications for patent term extension for certain of these patents. Our patent applications also include families relating in part to particular doses and dosing regimens for intravitreally or subcutaneously administered pegcetacoplan that are granted or pending in the United States and a number of other jurisdictions. Patents in these families would expire between 2036 and 2038. Four of our U.S. patents are listed for EMPAVELI in the FDA's Orange Book. Our filings also 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 the assets of Potentia Pharmaceuticals, Inc., or Potentia. These 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. We also own a patent family relating in part to use of C3 inhibitors, including pegcetacoplan, to facilitate gene therapy with AAV vectors. Patents in this family have terms extending into 2040.

In addition to the technology that we developed internally relating to compstatin analogs, we hold exclusive licenses from Penn, including a license agreement with Penn that was assigned to us in connection with our acquisition of the Potentia's assets in September 2015. The intellectual property in-licensed under our two license agreements with Penn includes four U.S. patents and numerous foreign counterparts, with claims granted in Europe, Japan and elsewhere. These licensed patent rights include issued patents with claims that recite a class of compounds generically covering pegcetacoplan and APL-9, and that specifically recite the active component. These patents have terms that extend to 2026.

We also own or have exclusive rights to a number of patent applications relating to additional modalities and molecules for inhibiting complement, including nucleic acid and protein-based approaches. The filings cover, for example, the composition of matter of our product candidates APL-1030 and APL-2006 and methods of use for treating particular complement-mediated disorders. Patents issuing based on these applications would have terms extending into 2041 or 2042.

We have a non-exclusive license to intellectual property covering aspects of base editing technology, including CRISPR proteins and base editors, for use in the context of our collaboration with Beam, and will have an exclusive license to intellectual property specifically covering therapeutic candidates developed under the collaboration.

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 worldwide rights to use and license the intellectual property that we hold with respect to pegcetacoplan and APL-9 to our wholly owned subsidiaries, APL DEL Holdings, LLC and Apellis Switzerland GmbH. Certain of our wholly owned subsidiaries hold rights to use our intellectual property to manage our clinical trials in certain jurisdictions or territories and exclusive rights to distribute our product with respect to specific indications within certain jurisdictions or territories. We granted Sobi an exclusive (subject to certain retained rights), sublicensable license of certain patent rights and know-how to develop and commercialize pegcetacoplan for non-ophthalmological indications in all countries outside of the United States.

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. Three of these patents are listed for EMPAVELI in the FDA's Orange Book.

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 January 2021 we made payments of $25,050,000 as sublicense fees under this agreement with respect to the Sobi collaboration and certain other strategic collaborations.

In August 2021 we made payments of $1,025,000, net of a credit for the annual license maintenance payment, for the achievement of milestones under this agreement. In December 2021, we recorded license costs of $5,000,000 related to the probable achievement of a milestone which we expect to be settled in the first half of 2022.

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. We accrued $0.3 million for royalty obligations to Penn in 2021.

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.

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

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

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

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

We have the right to grant sublicenses under the license.

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

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

Competition

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

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

Our approved product competes, and if our product candidates are approved for the indications for which we are currently undertaking or planning clinical trials, they will compete, with the products and product candidates discussed below

GA. There are currently no approved treatments for GA. We are aware that several companies that are actively developing product candidates for the treatment of GA, including the following product candidates that are in clinical development: ANX007, a C1q inhibitor being developed by Annexon Biosciences, Inc. in Phase 2 clinical trials; GT005, a CFI expression subretinal gene therapy being developed by Novartis in Phase 2 clinical trials (Novartis completed its acquisition of Gyroscope Therapeutics in February 2022); IONIS-FB-L(RX), a complement factor B inhibitor being developed by Ionis/Roche in Phase 2 clinical trials; Zimura (avacincaptad pegol), a C5 inhibitor being developed by Iveric Bio (in Phase 2/3 clinical trials; HMR59, an intravitreal gene therapy targeting CD59 being developed by The Janssen Pharmaceutical Companies of Johnson & Johnson (after acquisition from Hemera Biosciences) in Phase 2 clinical trials; NGM621, a C3 inhibitor being developed by NGM Biopharmaceuticals, Inc., in Phase 2 clinical trials; GEM103, a complement factor H targeting therapy being developed by Gemini Therapeutics, in Phase 2 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, Roche/Genentech, Lineage Cell Therapeutics, Inc., Regenerative Patch Technologies, LLC, and Stealth BioTherapeutics, Inc. Novartis has announced plans to initiate a Phase 2 trial of iptacopan, a Factor B inhibitor, in patients with early or intermediate AMD. AstraZeneca has announced plans to initiate a Phase 2 trial of orally delivered danicopan (ALXN2040) in GA.

PNH. The principal competitors for EMPAVELI, and possibly other indications in our hematology and nephrology programs are eculizumab (marketed as Soliris) and ravulizumab (marketed as Ultomiris), which are C5 inhibitors developed and marketed by AstraZeneca. In addition to EMPAVELI, 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 using complement inhibition for the treatment of PNH in late-stage clinical development, including BCX9930, a Factor D inhibitor being developed by BioCryst Pharmaceuticals, Inc., or BioCryst, currently in Phase 3 clinical trials; crovalimab, an anti-C5 antibody developed by Roche and Chugai Pharmaceutical Co., currently in Phase 3 clinical trials; pozelimab, an anti-C5 antibody developed by Regeneron Pharmaceuticals, Inc. in combination with cemdisiran, an RNAi therapeutic targeting C5 by Alnylam Pharmaceuticals, Inc., currently in Phase 3 clinical trials; danicopan, a Factor D inhibitor being developed by AstraZeneca as an add-on treatment to eculizumab and ravulizumab, in Phase 3 clinical trials; and iptacopan being developed by Novartis, currently in Phase 3 clinical trials, as well as other products in early stages of development.

Amgen Inc. is developing ABP959, a biosimilar for eculizumab that is in Phase 3 development, and other non-U.S. entities are developing biosimilars for eculizumab in local markets. 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.

CAD. Sutimlimab-jome, a C1s inhibitor monoclonal antibody developed by Sanofi was approved by the FDA in February 2022. Treatments in clinical development include iptacopan, an oral Factor B inhibitor, being developed by Novartis; and SAR445088, a C1s inhibitor monoclonal antibody, being developed by Sanofi.

C3G. There are currently no approved drugs for C3 glomerulopathy, but treatments in clinical development include iptacopan being developed by Novartis, currently in Phase 3 clinical trials; narsoplimab (OMS721), a MASP-2 inhibitor monoclonal antibody being developed by Omeros Corp., in a Phase 2 renal basket trial; avacopan, an oral C5aR-inhibitor developed by ChemoCentryx, Inc., in Phase 2 clinical trials; BCX9930, a Factor D inhibitor being developed by BioCryst, currently in a Phase 2 renal basket trial.

HSCT-TMA. Currently there are three treatments in clinical development: Ecluizumab, developed by AstraZeneca, nomacopan being developed by Akari, and narsoplimab, being developed by Omeros.

ALS. Currently there are four drug treatments approved by the FDA for treatment of ALS or its symptoms, including edaravone (marketed as Radicava by Mitsubishi Tanabe Pharma America; riluzole, now generic; thickened riluzole, marketed as Tiglutik by ITF Pharma, and dextromethorphan HBr/quinidine sulfate (marketed as Nuedexta by Avanir Pharmaceuticals). Various companies are conducting clinical trials for symptoms of, or neurological conditions, related to, ALS, with over 50 molecules currently in development that target a broad array of biology, including at least three other anti-complement therapies: Ultomiris by AstraZeneca, in Phase 3 trials, Zilucoplan by UCB/Ra in Phase 2 clinical trials, and ANX005 by Annexon Biosciences. Additionally, Amylyx Pharmaceuticals, Inc. recently submitted an NDA and an MAA for AMX0035 for the treatment of ALS.

Sales and Marketing

We retain U.S. commercialization rights for systemic pegcetacoplan and worldwide commercialization rights for intravitreal pegcetacoplan. We are conducting commercialization efforts for EMPAVELI in the United States and plan to conduct commercial development for systemic pegcetacoplan in the United States if it is approved in other indications. We have developed 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 particular, for PNH we have defined our marketing, disease education, patient support and distribution strategies, identified primary and secondary payers representing a significant percentage of patients with PNH, have built our field market access team and our sales team. Sobi is responsible for commercialization of systemic pegcetacoplan outside of the United States.

For our intravitreal pegcetacoplan program and for programs involving compounds other than pegcetacoplan, we plan to develop our own capabilities to commercialize our products worldwide. 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 and commercial sale. We have entered into a commercial supply agreement with Bachem Americas, Inc., or Bachem, agreeing to purchase a significant portion of our requirements for the pegcetacoplan drug substance over the next five years, and a commercial supply agreement with NOF Corporation, or NOF, to purchase activated polyethylene glycol derivative, or PEG, which is a component of pegcetacoplan. 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 and for commercial use 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 and for commercial use.

We believe that our manufacturing arrangements are sufficient to supply pegcetacoplan at the scale and with the quality required for our ongoing and planned clinical trials, our commercialization efforts and our collaboration with Sobi. We continuously review our supply chain risk, including with respect to our manufacturing footprint, and update and implement risk mitigation plans.

Commercial Supply Agreement with Bachem

On December 30, 2020, we entered into a commercial supply agreement, or the Bachem Agreement, with Bachem to supply the drug substance for the finished dosage form of pegcetacoplan for systemic and intravitreal administration.

Under the Bachem Agreement, we agreed to purchase from Bachem a significant portion of our requirements for the drug substance during the term of the agreement, and to purchase all of our requirements for drug substance for commercial sale, subject to certain exceptions, for a period after the effective date of the agreement.

Unless earlier terminated, the initial term of the Bachem Agreement continues for five years, or the Initial Term. Thereafter, the Bachem Agreement will automatically renew for an additional two-year term. At least 24 months prior to the end of the Initial Term, Bachem will notify us in writing if it is willing to continue to manufacture and supply the drug substance following the end of the Initial Term. For a period of 12 months after receipt of such notice, we have the right to negotiate pricing terms that would apply during the renewal term, which upon agreement will be finalized in an amendment to the Bachem Agreement. We may terminate the Bachem Agreement in the event any required license, permit or certificate of Bachem related to the manufacturing facility or the drug substance is not approved or issued (or is withdrawn) by the relevant governmental authority. Additionally, each party may terminate the Bachem Agreement upon an uncured material breach of the Bachem Agreement by the other party or upon the other party's insolvency or bankruptcy.

The Bachem Agreement also includes customary provisions relating to, among others, delivery, inspection procedures, warranties, quality, storage, handling and transport, intellectual property, confidentiality and indemnification.

Amended and Restated Commercial Supply Agreement with NOF

On March 10, 2021, we entered into an amended and restated commercial supply agreement, or the NOF Agreement, with NOF to purchase PEG, which is a component of pegcetacoplan.

Under the NOF Agreement, NOF's affiliate, NOF America Corporation, supplies PEG to us on a non-exclusive basis. NOF agreed to manufacture and deliver PEG to us in accordance with purchase orders issued by the us pursuant to the NOF Agreement. We may purchase PEG or any polyethylene glycol derivative from other third-party suppliers. Notwithstanding the foregoing, we agreed to purchase at least a minimum purchase obligation, which will be based on our 24-month rolling forecasts as set forth in the NOF Agreement. In the event we fail to meet the minimum purchase obligation, we will pay NOF the amount equal to a specified percentage of the remaining quantity of the minimum purchase obligation for the relevant time period, in addition to any payments due for all outstanding firm orders. We may eliminate the minimum purchase obligation on or before October 1 of the preceding calendar year by paying a specified percentage of the then-applicable supply price of the remaining minimum purchase obligation for the remainder of the term.

Unless earlier terminated, the term of the NOF Agreement continues through December 31, 2025. Either party may terminate the NOF Agreement upon an uncured material breach by the other party, upon the other party's insolvency or bankruptcy or for convenience upon twenty-four (24) months prior written notice. We may terminate the NOF Agreement for safety, efficacy or regulatory issues. If the NOF Agreement is terminated by NOF for convenience or by us for NOF's breach, we have no minimum purchase obligations and any agreement to buy out such minimum purchase obligations shall be of no force or effect.

The NOF Agreement also includes customary provisions relating to, among others, delivery, inspection procedures, warranties, quality, storage, handling and transport, intellectual property, confidentiality and indemnification.

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.

The regulatory requirements applicable to drug product development, approval and marketing are subject to change, and regulations and administrative guidance often are revised or reinterpreted by the agencies in ways that may have a significant impact on our business.

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 requirements under the FDCA and other applicable laws 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.

The FDA must approve our product candidates for therapeutic indications before they may be marketed in the United States. 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;
- design of a clinical protocol and 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 an 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 the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards and the U.S. Department of Agriculture's Animal Welfare Act, if applicable. 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 AEs 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 or recommence. Occasionally, clinical holds are imposed due to manufacturing issues that may present safety issues for the clinical study subjects.

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. Specifically, on April 28, 2008, the FDA amended its regulations governing the acceptance of foreign clinical studies not conducted under an IND application as support for an IND or an NDA. The final rule provides 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. The GCP requirements in the final rule encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

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 DSMB, 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.

Reporting Clinical Trial Results

Under the Public Health Service Act (the "PHSA"), sponsors of clinical trials of certain FDA-regulated products, including prescription drugs and biologics, are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health (the "NIH"). In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Although sponsors are also obligated to disclose the results of their clinical trials after completion, disclosure of the results can be delayed in some cases for up to two years after the date of completion of the trial. The NIH's Final Rule on registration and reporting requirements for clinical trials became effective in 2017, and both the NIH and the FDA have recently signaled the government's willingness to begin enforcing those requirements against non-compliant clinical trial sponsors.

Specifically, the PHSA grants the Secretary of Health and Human Services the authority to issue a notice of noncompliance to a responsible party for failure to submit clinical trial information as required. The responsible party, however, is allowed 30 days to

correct the noncompliance and submit the required information. The failure to submit clinical trial information to clinicaltrials.gov, as required, is also a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues. In addition to civil monetary penalties, violations may also result in other regulatory action, such as injunction and/or criminal prosecution or disqualification from federal grants. Although the FDA has historically not enforced these reporting requirements due to the Department of Health and Human Services' (the "HHS") long delay in issuing final implementing regulations, those regulations have now been issued and the FDA did issue its first Notice of Noncompliance to a manufacturer in April 2021.

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.

There is no obligation for a sponsor to make its investigational products available for expanded access; however, as required by amendments to the FDCA included in the 21st Century Cures Act (the "Cures Act"), passed in 2016, if a sponsor has a policy regarding how it responds to expanded access requests with respect to product candidates in development to treat serious diseases or conditions, it must make that policy publicly available. 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 investigational drug or biologic receives designation from the FDA 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 Trials 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. Each protocol, and any subsequent material amendment to the protocol, must be submitted to the FDA as part of the IND, and progress reports detailing the status of the clinical trials must be submitted to the FDA annually.

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. These clinical trials are commonly referred to as "pivotal" studies, which denotes a study that presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a drug.

- 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.

A clinical trial may combine the elements of more than one phase and the FDA often requires more than one Phase 3 trial to support marketing approval of a product candidate. A company's designation of a clinical trial as being of a particular phase is not necessarily indicative that the study will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA. Moreover, as noted above, a pivotal trial is a clinical trial that is believed to satisfy FDA requirements for the evaluation of a product candidate's safety and efficacy such that it can be used, alone or with other pivotal or non-pivotal trials, to support regulatory approval. Generally, pivotal trials are Phase 3 trials, but they may be Phase 2 trials if the design provides a well-controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need.

In response to the COVID-19 pandemic, the FDA issued guidance on March 18, 2020, and has updated it periodically since that time to address the conduct of clinical trials during the pandemic. The guidance sets out a number of considerations for sponsors of clinical trials impacted by the pandemic, including the requirement to include in the clinical study report (or as a separate document) contingency measures implemented to manage the study, and any disruption of the study as a result of COVID-19; a list of all study participants affected by COVID-19-related study disruptions by a unique subject identifier and by investigational site, and a description of how the individual's participation was altered; and analyses and corresponding discussions that address the impact of implemented contingency measures (e.g., participant discontinuation from investigational product and/or study, alternative procedures used to collect critical safety and/or efficacy data) on the safety and efficacy results reported for the study, among other things. The FDA has indicated that it will continue to provide any necessary guidance to sponsors, clinical investigators, and research institutions as the public health emergency evolves.

Interactions with FDA During the Clinical Development Program

Following the clearance of an IND and the commencement of clinical trials, the sponsor will continue to have interactions with the FDA. 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. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

In addition, sponsors are given opportunities to meet with the FDA at certain points in the clinical development program. Specifically, sponsors may meet with the FDA prior to the submission of an IND (Pre-IND meeting), at the end of Phase 2 clinical trial (EOP2 meeting) and before an NDA is submitted (Pre-NDA meeting). Meetings at other times may also be requested. There are four types of meetings that occur between sponsors and the FDA. Type A meetings are those that are necessary for an otherwise stalled product development program to proceed or to address an important safety issue. Type B meetings include pre-IND and pre-NDA meetings, as well as end of phase meetings such as EOP2 meetings. A Type C meeting is any meeting other than a Type A or Type B meeting regarding the development and review of a product, including for example meetings to facilitate early consultations on the use of a biomarker as a new surrogate endpoint that has never been previously used as the primary basis for product approval in the proposed context of use.

These meetings provide an opportunity for the sponsor to share information about the data gathered to date with the FDA and for the FDA to provide advice on the next phase of development. For example, at an EOP2, a sponsor may discuss its Phase 2 clinical results and present its plans for the pivotal Phase 3 clinical trial(s) that it believes will support the approval of the new product. Such meetings may be conducted in person, via teleconference/videoconference or written response only with minutes reflecting the questions that the sponsor posed to the FDA and the agency's responses. The FDA has indicated that its responses, as conveyed in meeting minutes and advice letters, only constitute mere recommendations and/or advice made to a sponsor and, as such, sponsors are not bound by such recommendations and/or advice. Nonetheless, from a practical perspective, a sponsor's failure to follow the FDA's recommendations for design of a clinical program may put the program at significant risk of failure.

Manufacturing and Other Regulatory Requirements

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.

Specifically, the FDA's regulations require that pharmaceutical products be manufactured in specific approved facilities and in accordance with cGMPs. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports and returned or salvaged products. Manufacturers and other entities involved in the manufacture and distribution of approved pharmaceuticals are required to register their establishments with the FDA and some state agencies, and they are subject to periodic unannounced inspections by the FDA for compliance with cGMPs and other requirements. Inspections must follow a "risk-based schedule" that may result in certain establishments being inspected more frequently. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to be adulterated. Changes to the manufacturing process, specifications or container closure system for an approved product are strictly regulated and often require prior FDA approval before being implemented. The FDA's regulations also require, among other things, the investigation and correction of any deviations from cGMP and the imposition of reporting and documentation requirements upon the sponsor and any third-party manufacturers involved in producing the approved product.

Pediatric Studies

Under the Pediatric Research Equity Act (the "PREA") applications and certain types of supplements to applications must contain data that are adequate to assess the safety and effectiveness of the 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. The sponsor must submit an initial Pediatric Study Plan ("PSP") within 60 days of an end-of-phase 2 meeting or as may be agreed between the sponsor and the FDA. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The sponsor and the FDA must reach agreement on a final plan. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials, and/or other clinical development programs.

For investigational products intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of an applicant, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, the FDA will meet early in the development process to discuss pediatric study plans with sponsors, and the FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than ninety days after the FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation, although FDA has recently taken steps to limit what it considers abuse of this statutory exemption in PREA by announcing that it does not intend to grant any additional orphan drug designations for rare pediatric subpopulations of what is otherwise a common disease. The FDA also maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population.

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.

Acceptance and Review of NDAs

Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, along with information relating to the product's chemistry, manufacturing, controls, safety updates, patent information, abuse information and proposed labeling, are submitted to the FDA as part of an application requesting approval to market the product candidate for one or more indications. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data

submitted must be sufficient in quality and quantity to establish the safety and efficacy of a drug product. The fee required for the submission and review of an application under the Prescription Drug User Fee Act (the "PDUFA"), is substantial (for example, for fiscal year 2022 this application fee is approximately $3.1 million), and the sponsor of an approved application is also subject to an annual program fee, currently more than $369,000 per eligible prescription product. These fees are typically adjusted annually, and exemptions and waivers may be available under certain circumstances, such as where a waiver is necessary to protect the public health, where the fee would present a significant barrier to innovation, or where the applicant is a small business submitting its first human therapeutic application for review.

The FDA conducts a preliminary review of all applications within 60 days of receipt and must inform the sponsor at that time or before whether an application is sufficiently complete to permit substantive review. In pertinent part, the FDA's regulations state that an application "shall not be considered as filed until all pertinent information and data have been received" by the FDA. In the event that FDA determines that an application does not satisfy this standard, it will issue a Refuse to File ("RTF") determination to the applicant. Typically, an RTF will be based on administrative incompleteness, such as clear omission of information or sections of required information; scientific incompleteness, such as omission of critical data, information or analyses needed to evaluate safety and efficacy or provide adequate directions for use; or inadequate content, presentation, or organization of information such that substantive and meaningful review is precluded. The FDA may request additional information rather than accept an application 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.

After the submission is accepted for filing, the FDA begins an in-depth substantive review of the application. The FDA reviews the application to determine, among other things, whether the proposed product is safe and effective for its intended use, whether it has an acceptable purity profile and whether the product is being manufactured in accordance with cGMP. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has ten months from the filing date in which to complete its initial review of a standard application that is a new molecular entity, and six months from the filing date for an application with "priority review." The review process may be extended by the FDA for three additional months to consider new information or in the case of a clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission. Despite these review goals, it is not uncommon for FDA review of an application to extend beyond the PDUFA goal date.

In connection with its review of an application, the FDA will typically submit information requests to the applicant and set deadlines for responses thereto. The FDA will also conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether the manufacturing processes and facilities comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the product within required specifications. The FDA also may inspect the sponsor and one or more clinical trial sites to assure compliance with IND and GCP requirements and the integrity of the clinical data submitted to the FDA. To ensure cGMP and GCP compliance by its employees and third-party contractors, an applicant may incur significant expenditure of time, money and effort in the areas of training, record keeping, production and quality control.

Additionally, the FDA may refer an application, including applications for novel product candidates which present difficult questions of safety or efficacy, to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. 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 recommendation of an advisory committee, but it considers such recommendations when making final decisions on approval. Data from clinical trials are not always conclusive, and the FDA or its advisory committee may interpret data differently than the sponsor interprets the same data. The FDA may also re-analyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process.

The FDA also may require submission of a REMS if it determines that a REMS is necessary to ensure that the benefits of the product outweigh its risks and to assure the safe use of the product. The REMS could include medication guides, physician communication plans, assessment plans and/or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools. The FDA determines the requirement for a REMS, as well as the specific REMS provisions, on a case-by-case basis. If the FDA concludes a REMS is needed, the sponsor of the application must submit a proposed REMS and the FDA will not approve the application without a REMS.

Decisions on NDAs

The FDA reviews an applicant to determine, among other things, whether the product is safe and whether it is effective for its intended use(s), with the latter determination being made on the basis of substantial evidence. The term "substantial evidence" is defined under the FDCA as "evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the product involved, on the basis of which it could fairly and responsibly be concluded by such experts that the product will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof."

The FDA has interpreted this evidentiary standard to require at least two adequate and well-controlled clinical investigations to establish effectiveness of a new product. Under certain circumstances, however, the FDA has indicated that a single trial with certain characteristics and additional information may satisfy this standard. This approach was subsequently endorsed by Congress in 1998 with legislation providing, in pertinent part, that "If [FDA] determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the FDA may consider such data and evidence to constitute substantial evidence." This modification to the law recognized the potential for the FDA to find that one adequate and well controlled clinical investigation with confirmatory evidence, including supportive data outside of a controlled trial, is sufficient to establish effectiveness. In December 2019, the FDA issued draft guidance further explaining the studies that are needed to establish substantial evidence of effectiveness. It has not yet finalized that guidance.

After evaluating the application and all related information, including the advisory committee recommendations, if any, and inspection reports of manufacturing facilities and clinical trial sites, the FDA will issue either a Complete Response Letter ("CRL") or an approval letter. To reach this determination, the FDA must determine that the drug is effective and that its expected benefits outweigh its potential risks to patients. This "benefit-risk" assessment is informed by the extensive body of evidence about the product's safety and efficacy in the NDA. This assessment is also informed by other factors, including: the severity of the underlying condition and how well patients' medical needs are addressed by currently available therapies; uncertainty about how the premarket clinical trial evidence will extrapolate to real-world use of the product in the post-market setting; and whether risk management tools are necessary to manage specific risks. In connection with this assessment, the FDA review team will assemble all individual reviews and other documents into an "action package," which becomes the record for FDA review. The review team then issues a recommendation, and a senior FDA official makes a decision.

A CRL indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A CRL generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. The CRL may require additional clinical or other data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time- consuming requirements related to clinical trials, preclinical studies or manufacturing. If a CRL is issued, the applicant will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the applicant an additional six-month extension to respond.

The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with the submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. The FDA has taken the position that a CRL is not final agency action making the determination subject to judicial review.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications. That is, the approval will be limited to the conditions of use (e.g., patient population, indication) described in the FDA-approved labeling. Further, depending on the specific risk(s) to be addressed, the FDA may 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.

Under the Ensuring Innovation Act, which was signed into law in April 2021, the FDA must publish action packages summarizing its decisions to approve new drugs within 30 days of approval of such products. To date, CRLs are not publicly available documents.

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 a variety of federal and state laws, the most recent of which is still in the process of being phased into the U.S. supply chain and regulatory framework. The Prescription Drug Marketing Act (the "PDMA") was the first federal law to set minimum standards for the registration and regulation of drug distributors by the states and to regulate the distribution of drug samples. Today, both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. Congress more recently enacted the Drug Supply Chain Security Act (the "DSCSA"), which made significant amendments to the FDCA, including by replacing certain provisions from the PDMA pertaining to wholesale distribution of prescription drugs with a more comprehensive statutory scheme. The DSCSA now requires uniform national standards for wholesale distribution and, for the first time, for third-party logistics providers; it also provides for preemption of certain state laws in the areas of licensure and prescription drug traceability.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the applicant to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the applicant for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval

for new or improved formulations or new uses of previously approved products. If the Section 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Generic Drugs and Regulatory Exclusivity

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 or 505(b)(2) application 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. This interpretation was confirmed with enactment of the Ensuring Innovation Act in April 2021. 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, a generic or follow-on drug application 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.

The FDA must establish a priority review track 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

As part of the submission of an NDA or certain supplemental applications, 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. Upon approval of a new drug, each of the patents listed in the application for the drug is then published in the Orange Book. The FDA's regulations governing patent listings were largely codified into law with enactment of the Orange Book Modernization Act in January 2021.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.

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. As a result, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of an NCE, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Pediatric 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. PMA applications are subject to an application fee. For federal fiscal year 2021, the standard fee is $365,657 and the small business fee is $91,414.

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 addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products outside of the United States. Whether or not we obtain FDA approval for a product candidate, we must obtain approval by the comparable regulatory authorities of foreign countries or economic areas, such as the 27-member EU, before we may commence clinical trials or market products in those countries or areas. In the EU, our product candidates also may be subject to extensive regulatory requirements. As in the United States, medicinal products can be marketed only if a marketing authorization from the competent regulatory agencies has been obtained. Similar to the United States, the various phases of preclinical and clinical research in the EU are subject to significant regulatory controls.

With the exception of the EU/European Economic Area ("EEA") applying the harmonized regulatory rules for medicinal products, the approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly 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.

Clinical Trial Approval

The Clinical Trials Directive 2001/20/EC, the Directive 2005/28/EC on GCP and the related national implementing provisions of the individual EU Member States govern the system for the approval of clinical trials in the EU. Under this system, an applicant must obtain prior approval from the competent national authority of the EU Member States in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by, among other documents, an IMPD (the Common Technical Document) with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC, and where relevant the implementing national provisions of the individual EU Member States and further detailed in applicable guidance documents. All suspected unexpected serious adverse reactions to the investigational drug product that occur during the clinical trial have to be reported to the competent national authority and the Ethics Committee of the Member State where they occurred.

In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014 ("Clinical Trials Regulation") was adopted. The Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the EU. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the "EU portal"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned). Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

The new Regulation is scheduled to come into application on January 31, 2022, following confirmation of full functionality of the Clinical Trials Information System through an independent audit by the European Commission in mid-2020. The Clinical Trials Regulation will come into application in all the EU Member States, repealing the current Clinical Trials Directive 2001/20/EC. The conduct of all clinical trials performed in the EU will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable at the end of January 2022. According to the transitional provisions, if a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable, the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

Parties conducting certain clinical trials must, as in the United States, post clinical trial information in the EU at the EudraCT website: https://eudract.ema.europa.eu.

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.

Within this framework, manufacturers may seek approval of hybrid medicinal products under Article 10(3) of Directive 2001/83/EC. Hybrid applications rely, in part, on information and data from a reference product and new data from appropriate preclinical tests and clinical trials. Such applications are necessary when the proposed product does not meet the strict definition of a generic medicinal product, or bioavailability studies cannot be used to demonstrate bioequivalence, or there are changes in the active substance(s), therapeutic indications, strength, pharmaceutical form or route of administration of the generic product compared to the reference medicinal product. In such cases the results of tests and trials must be consistent with the data content standards required in the Annex to the Directive 2001/83/EC, as amended by Directive 2003/63/EC.

Hybrid medicinal product applications have automatic access to the centralized procedure when the reference product was authorized for marketing via that procedure. Where the reference product was authorized via the decentralized procedure, a hybrid application may be accepted for consideration under the centralized procedure if the applicant shows that the medicinal product constitutes a significant therapeutic, scientific or technical innovation, or the granting of a community authorization for the medicinal product is in the interest of patients at the community level.

Pediatric Studies in the EU

Prior to obtaining a marketing authorization in the European Union, applicants must demonstrate compliance with all measures included in an EMA-approved PIP covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are laid down in Regulation (EC) No 1901/2006, the so-called Paediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Paediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine for children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine in children is not needed or is not appropriate because (a) the product is likely to be ineffective or unsafe in part or all of the pediatric population; (b) the disease or condition occurs only in adult population; or (c) the product does not represent a significant therapeutic benefit over existing treatments for pediatric population. Before an MAA can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP.

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.

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 with respect to 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 EC 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 EU 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).

Regulatory Requirements after Marketing Authorization

As in the U.S., both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual EU Member States both before and after grant of the manufacturing and marketing authorizations. The holder of an EU marketing authorization for a medicinal product must, for example, comply with EU pharmacovigilance legislation and its related regulations and guidelines which entail many requirements for conducting pharmacovigilance, or the assessment and monitoring of the safety of medicinal products. The manufacturing process for medicinal products in the EU is also highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, including compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients.

In the EU, the advertising and promotion of approved products are subject to EU Member States' laws governing promotion of medicinal products, interactions with clinicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU Member States may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics ("SmPC") as approved by the competent authorities. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion, which is prohibited in the EU.

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.

Orphan Drug Designation and Exclusivity

The criteria for designating an orphan medicinal product in the EU are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition, (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition. The term 'significant benefit' is defined in Regulation (EC) 847/2000 to mean a clinically relevant advantage or a major contribution to patient care.

Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. During this ten-year market exclusivity period, the EMA or the competent authorities of the Member States of the EEA, cannot accept an application for a marketing authorization for a similar medicinal product for the same indication. A similar medicinal product is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The application for orphan designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the marketing authorization application if the orphan designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The ten-year market exclusivity in the EU may 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 designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if: (1) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (2) the applicant consents to a second orphan medicinal product application; or (3) the applicant cannot supply enough orphan medicinal product.

Pediatric Exclusivity in the EU

If an applicant obtains a marketing authorization in all EU Member States, or a marketing authorization granted in the centralized procedure by the European Commission, and the study results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six-month period of qualifying patent protection through extension of the term of the Supplementary Protection Certificate, or SPC, or alternatively a one year extension of the regulatory market exclusivity from ten to eleven years, as selected by the marketing authorization holder.

Patent Term Extensions

The EU also provides for patent term extension through SPCs. The rules and requirements for obtaining a SPC are similar to those in the United States. An SPC may extend the term of a patent for up to five years after its originally scheduled expiration date and can provide up to a maximum of fifteen years of marketing exclusivity for a drug. In certain circumstances, these periods may be extended for six additional months if pediatric exclusivity is obtained. Although SPCs are available throughout the EU, sponsors must apply on a country-by-country basis. Similar patent term extension rights exist in certain other foreign jurisdictions outside the EU.

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). On December 24, 2020, the United Kingdom and the European Union entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. 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, as the United Kingdom legislation now has the potential to diverge from European Union legislation. It remains to be seen how Brexit will impact regulatory requirements for product candidates and products in the UK in the long-term. The MHRA has recently published detailed guidance for industry and organizations to follow from January 1, 2021 now the transition period is over, which will be updated as the UK's regulatory position on medicinal products evolves over time.

Furthermore, while the Data Protection Act of 2018 in the United Kingdom that "implements" and complements the European Union's General Data Protection Regulation, or GDPR, has achieved Royal Assent on May 23, 2018 and is now effective in the United Kingdom, it is still unclear whether transfer of data from the European Economic Area, or EEA, to the United Kingdom will remain lawful under GDPR. The Trade and Cooperation Agreement provides for a transitional period during which the United Kingdom will be treated like an European Union member state in relation to processing and transfers of personal data for four months from January 1, 2021. This may be extended by two further months. After such period, the United Kingdom will be a "third country" under the GDPR unless the European Commission adopts an adequacy decision in respect of transfers of personal data to the United Kingdom. The United Kingdom has already determined that it considers all of the EU 27 and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the United Kingdom to the EU/EEA remain unaffected.

General Data Protection Regulation

Many countries outside of the United States maintain rigorous laws governing the privacy and security of personal information. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data regarding individuals who are located in the EEA, and the processing of personal data that takes place in the EEA, 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 sensitive personal data relates before processing such data. Examples of obligations imposed by the GDPR on companies processing personal data that falls within the scope of the GDPR include, 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 is 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. In July 2020, the Court of Justice of the EU, or the CJEU, invalidated the EU-U.S. Privacy Shield framework, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the United States. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the United States. Following the withdrawal of the

U.K. from the EU, the U.K. Data Protection Act 2018 applies to the processing of personal data that takes place in the U.K. and includes parallel obligations to those set forth by GDPR.

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, health outcome studies in order to demonstrate the medical necessity, quality of life benefits, 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 in light of cost-benefit analysis. Additionally, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development.

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

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

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 in order to obtain reimbursement. 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 and issue guidance to prescribers. 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, reference pricing and 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. This legislation resulted in aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which will remain in effect through 2031. However, pursuant to the CARES Act and subsequent legislation, these Medicare sequester reductions are suspended through the end of March 2022 and from April 2022 through June 2022, a 1% cut will be in effect, with the full 2% cut resuming thereafter. These 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.

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. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden

rescinded those orders and issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. This Executive Order also directs the U.S. Department of Health and Human Services to create a special enrollment period for the Health Insurance Marketplace in response to the COVID-19 pandemic. We cannot predict how federal agencies will respond to such Executive Orders.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States To date, there have been several recent U.S. congressional inquiries, as well as 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. To those ends, the Trump Administration issued five executive orders intended to lower the costs of prescription drug products but it is unclear whether, and to what extent, these orders will remain in force under the Biden Administration. Further, on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has 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 organizations 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.

Employees and Human Capital

As of December 31, 2021, we had 476 full-time employees. Of these employees, 448 were based in the United States and 28 were based in international locations and 42 held Ph.D., Pharm.D. or M.D. degrees. None of our employees are represented by a labor union or covered under a collective bargaining agreement. We also retain independent contractors to support the goals of our organization. We are committed to providing a positive employee experience and a culture that embodies our values.

Fostering a diverse and inclusive culture which invests in attracting, retaining, engaging and developing our people is critical to achieving our business objectives and bringing value to patients, shareholders and all stakeholders. We are a majority female organization, and we maintain significant female representation at all levels. As of December 31, 2021, 57% of our workforce were women and 34% represented in senior leadership roles. Racial and ethnic diversity in the aggregate has improved at our company over the last few years. As of December 31, 2021, 25% of our workforce were ethnically diverse and 6.8% represented in senior leadership roles. However, we recognize that there is still important progress to be made, particularly as relates to Black and Latino representation at our company, and this remains an area of continued emphasis for us.

To incentivize and reward strong performance, we have a competitive compensation and benefits programs, including short-term and long-term incentives, exceptional health and wellness benefits along with generous vacation and leave programs.

We regularly evaluate the effectiveness of our talent management practices through employee surveys and fostering a culture of ongoing feedback. In addition, we track important talent metrics such as turnover rate and employee engagement. Voluntary and involuntary turnover rates across all levels (executives/ senior managers, mid-level managers and professionals) are in alignment with, or lower than, the industry average.

Since the onset of the COVID-19 pandemic, we demonstrated our commitment to the health and wellbeing of our employees, our patients and our community upholding local and federal public health guidelines. With input from our employees, we developed a new working model. This new model includes:

- Standard operating procedures designed to protect the health and well-being of our team and communities.
- Flexibility for employees to balance their preferred work arrangements (on-site, partially on-site, or fully remote) with business needs.
- Adapted office settings to enable difference work experiences ensuring safe space for collaboration, social and communal engagement, and appropriate space for larger group meetings.

- Adopted technology and operating practices to support communicating and collaborating as a hybrid workforce reinforcing our values.
- Invested in wellness programs and resources to help employees balance work-life throughout the pandemic and beyond.

Corporate Information

Our principal executive office is located at 100 Fifth Avenue, Waltham, Massachusetts, and our telephone number is 617-977-5700.

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 this year and next year, 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 net operating losses for at least this year and next year. Our net losses were $746.4 million, $344.9 million and $304.7 million for the years ended December 31, 2021, 2020 and 2019, respectively. As of December 31, 2021, we had an accumulated deficit of $1.7 billion. While we have begun to generate revenue from sales of EMPAVELI, we have primarily financed our operations to date 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 prior to our initial public offering, the development funding agreement with SFJ Pharmaceuticals Group, or SFJ, the collaboration agreement with Swedish Orphan Biovitrum AB (Publ), or Sobi, 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 across several disease indications and preparing for the commercial launch of EMPAVELI for the treatment of adults with PNH in the United States. 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:

- establish sales, marketing, distribution and other commercial infrastructure to commercialize any products for which we may obtain marketing approval;
- continue the commercial launch of EMPAVELI for the treatment of PNH in the United States;
- prepare to submit applications for regulatory approval and build a commercial infrastructure for intravitreal pegcetacoplan for GA in the United States and worldwide;

- continue our efforts to establish a sales, marketing, distribution and other commercial infrastructure in connection with the commercialization of EMPAVELI and any other products for which we may obtain marketing approval;
- continue to develop and conduct clinical trials of pegcetacoplan and future product candidates, 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;
- 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 significant revenue. The ability to generate this revenue will require us to successful commercialize EMPAVELI and, if we obtain regulatory approval, intravitreal pegcetacoplan. While we began to generate revenue from sales of EMPAVELI in May 2021, there can be no assurance that we will generate significant revenue or as to the timing of any such revenue, and we may not achieve profitability for several years, if at all.

EMPAVELI is the only product for which we have obtained marketing approval and it has only been approved in the United States for the treatment of PNH in adults. Our ability to generate revenue from operations will depend, in part, on the timing and success of commercial sales of EMPAVELI. We may not be able to commercialize EMPAVELI successfully or on the expected timeline. However, the successful commercialization of EMPAVELI in the United States is subject to many risks. There are numerous examples of unsuccessful product launches and failures to meet expectations of market potential, including by pharmaceutical companies with more experience and resources than us. We do not anticipate our revenue from sales of EMPAVELI for the treatment of PNH alone will be sufficient for us to become profitable for several years, if at all, including if we obtain additional marketing approvals for EMPAVELI outside of the United States and European Union.

Our long-term prospects depend upon the success of our intravitreal pegcetacoplan program, among other things. We plan to submit a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, in the second quarter of 2022 for the approval of intravitreal pegcetacoplan for the treatment of geographic atrophy, or GA, which submission would be supported by the completed Phase 2 and Phase 3 clinical trials of intravitreal pegcetacoplan in patients with GA. Any delay in submitting the NDA, or adverse action by the FDA, could delay our planned commercial development timelines or could prevent us from commercializing intravitreal pegcetacoplan. If the FDA determines that our NDA and the data supporting the NDA are not sufficient to support approval in GA, we may be required to conduct an additional clinical trial, which would increase our costs and delay the program. Any such delay or other adverse impact could have a material adverse effect on our business.

We do not expect to generate significant revenue unless and until we and our collaborators, including Sobi, are able to obtain marketing approval for, and successfully commercialize pegcetacoplan in additional indications and jurisdictions. 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 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 collaborators may never succeed in these activities and, even if we do, or any 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 obtained marketing approval for EMPAVELI for the treatment of PNH in the United States and have not yet consistently demonstrated an ability to successfully conduct commercial activities.

We obtained our first marketing approval for the use of pegcetacoplan to treat adult patients with PNH in the United States and began to sell EMPAVELI for the treatment of PNH in May 2021. Our collaborator Sobi recently obtained marketing approval in the European Union, Saudi Arabia and Australia for the use of pegcetacoplan to treat patients with PNH. We have not obtained marketing approval nor commercialized any other products for any other indications, all of which may make it difficult to evaluate our future prospects. Prior to obtaining these approvals, our operations were limited to financing and staffing our company, developing our technology, conducting preclinical research and clinical trials of our product candidates and preparing for a commercial launch. We have not yet consistently 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 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 need to continue 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 to allow us to support both our systemic and ophthalmological programs through clinical development and commercial launch, 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, 2021, 2020 and 2019, we used net cash of $563.1 million, $160.5 million and $211.1 million respectively, in our operating activities substantially all of which related to research and development activities. As of December 31, 2021, our cash, cash equivalents and marketable securities were $700.6 million. We expect our expenses to increase, particularly as we commercialize EMPAVELI, seek regulatory approval and develop commercial infrastructure for intravitreal pegcetacoplan and initiate new clinical trials and initiate new research and preclinical development efforts. In addition, as we commercialize EMPAVELI and if we obtain marketing approval of pegcetacoplan in other indications or jurisdictions or for our other product candidates, we will 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 the collaborator. Furthermore, we continue to 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, particularly if we are able to obtain marketing approval of intravitreal pegcetacoplan for the treatment of GA and we commercialize it outside the United States without a collaborator or if we fail to establish substantial commercial sales of EMPAVELI. 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 our 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 to our collaboration agreement with Sobi, we may seek one or more additional collaborators for future development of our product candidates for one or more indications. However, we may not be able to enter into an additional collaboration for any of our product candidates for such indications on suitable terms, on a timely basis or at all. Accordingly, we may 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 other than Sobi's reimbursement obligations under the collaboration agreement. 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, cash equivalents and marketable securities, along with the cash anticipated to be generated from sales of EMPAVELI and the first regulatory milestone payment and committed development reimbursement payments from Sobi, will enable us to fund our operating expenses and capital expenditure requirements at least into the second quarter of 2023. Our estimate as to how long we expect our cash, cash equivalents and marketable securities 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. We plan to devote substantial resources to the preparation of submission for regulatory approval and to the building of a commercial infrastructure for intravitreal pegcetacoplan for GA and to the development of our other product candidates. We will seek additional funding to conduct these activities. 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:

- our ability to successfully commercialize and sell EMPAVELI in the United States;
- the cost and our ability to submit applications for regulatory approval and to build a commercial infrastructure for intravitreal pegcetacoplan for GA in the United States and worldwide;
- the cost and our ability to effectively establish and maintain the commercial infrastructure and manufacturing capabilities required to support the commercialization of EMPAVELI, intravitreal pegcetacoplan and any other products for which we receive marketing approval including product sales, medical affairs, marketing, manufacturing and distribution;
- the scope, progress, timing, costs and results of clinical trials of, and research and preclinical development efforts for EMPAVELI, systemic pegcetacoplan, intravitreal pegcetacoplan and other product candidates;
- our ability to maintain a productive collaborative relationship with Sobi with respect to systemic pegcetacoplan, including our ability to achieve milestone payments under our agreement with Sobi;
- our ability to identify additional collaborators 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 of pegcetacoplan in other jurisdictions and indications and other product candidates we may pursue;
- 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 our 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 pegcetacoplan in other jurisdictions and indications and our other 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;
- the effect of the COVID-19 pandemic on the healthcare system and the economy generally and on our clinical trials and other operations specifically;
- our ability to obtain adequate reimbursement for EMPAVELI in the United States or any other 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, following approval by the FDA and the EMA for the use of pegcetacoplan as a treatment for PNH, we paid SFJ initial payments of $4.0 million in 2021 and $5.0 million in 2022, respectively, and we are obligated to pay an aggregate of $451.0 million in six additional annual payments with the majority of the payments being made from the third anniversary to the sixth anniversary of regulatory approval.

Additionally, we granted a security interest to SFJ 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.

In January 2021, we closed privately negotiated exchanges with holders of our outstanding 2019 Convertible Notes, under which we issued approximately 3.9 million shares of common stock in exchange for approximately $126.1 million in aggregate principal amount of 2019 Convertible Notes.

In July 2021, we closed additional privately negotiated exchanges with holders of the outstanding Convertible Notes, under which we issued approximately 6.0 million shares of common stock in exchange for approximately $201.1 million in aggregate principal amount of Convertible Notes. The effective price per share of the common stock issued in the exchange transactions was lower than the trading price of our common stock on the Nasdaq Global Select Market at the time of settlement of the exchanges. We may in the future exchange additional principal amount of our Convertible Notes and the effective price per share of the common stock may be lower than the trading price at such time.

During the quarter ended September 30, 2021, the Convertible Notes were convertible at the option of the holders, and certain holders of the Convertible Notes converted approximately $0.7 million of aggregate principal amount of Convertible Notes into an aggregate of 18,775 shares. The shares were issued in October 2021.

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.

We are required to make substantial payments to SFJ pursuant to our development funding agreement as a result of receiving regulatory approval of EMPAVELI for the treatment of PNH. 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.

We submitted an NDA to the FDA and an MAA to the EMA for pegcetacoplan for the treatment of patients with PNH in September 2020. We received FDA approval of EMPAVELI for the treatment of patients with PNH in May 2021 and we received approval from the European Commission (EC) for Aspaveli in December 2021. We are required to make substantial payments to SFJ pursuant to our development funding agreement as a result of obtaining these regulatory approvals. Our ability to make these required payments depends on our future performance and the future performance of Sobi, 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 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 an aggregate of $520.0 million of indebtedness as a result of the issuance of convertible notes in September 2019 and May 2020, or the Convertible Notes, of which an aggregate of approximately $192.0 million is outstanding and held by third parties as of December 31, 2021. 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. The conditional conversion feature of the Convertible Notes was triggered as of June 30, 2021, and so the Notes were convertible at the option of the holders, in whole or in part, between July 1, 2021 and September 30, 2021. Whether the Convertible Notes will be convertible in any future period will depend on the satisfaction of this condition or another conversion condition at such time. In addition, even if holders do not elect to convert their Convertible Notes during a period when the notes are convertible, 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.

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

The COVID-19 pandemic may affect our ability to initiate and complete preclinical studies and conduct our ongoing clinical trials, delay the initiation of planned and future clinical trials, disrupt regulatory activities, or have other adverse effects on our business and operations. In addition, this pandemic has adversely impacted economies worldwide, which could result in adverse effects on our business and operations.

The COVID-19 pandemic has caused many governments to implement measures to slow the spread of the outbreak through quarantines, strict travel restrictions, heightened border scrutiny, and other measures. The outbreak and government measures taken in response have had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. The future progression of the pandemic and its effects on our business and operations are uncertain.

We have re-opened our facilities, but many of our employees continue to work remotely part of the time.

We have enrolled, and seek to enroll, patients in our ongoing clinical trials at sites located both in the United States and internationally. We may face difficulties recruiting and retaining patients in our ongoing clinical trials because of logistical effects arising from the pandemic, including increased difficulty for patients and health care providers to travel to or access clinical sites. In particular, we believe that COVID-19 may have impacted enrollment in certain of our clinical studies, including the Phase 2 MERIDIAN trial that we are conducting in patients with ALS. If patients enrolled in our clinical trials are unable or unwilling to visit clinical trial sites, the data generated by the trials and the timing of completion of our clinical trials may be adversely affected particularly in clinical trials like DERBY and OAKS where patients are expected to travel to clinical sites on a monthly basis over an extended period of time. We may also face disruptions related to the ability to obtain necessary regulatory, institutional review board, or IRB, or other necessary site approvals, as well as other delays at clinical trial sites. In particular, site initiation, participant recruitment and enrollment, participant dosing, availability of drug product or clinical and laboratory supplies, distribution of clinical trial materials, study monitoring, and data analysis may be paused or delayed due to changes in hospital or university policies, federal, state or local regulations, prioritization of hospital resources toward pandemic efforts, or other reasons related to the pandemic. The potential suspension of clinical trial activity at clinical trial sites may have an adverse impact on our clinical trial plans and timelines.

Treatment with complement inhibitors, like pegcetacoplan and APL-9, has immunosuppressive effects. Elderly patients or patients with significantly compromised health, such as those in our clinical trials, could be more susceptible to infections and other complications as a result of treatment with complement inhibitors. The COVID-19 pandemic could lead to delayed enrollment in our trials, more frequent missed visits from ongoing trials and more frequent or severe adverse events during our trials.

We also may face disruptions as a result of the COVID-19 pandemic that affect our ability to procure items that are essential for our research and development activities, including, for example, raw materials used in the manufacturing of our product candidates and laboratory and clinical supplies for our clinical trials. If we experience supply issues, our clinical trial plans and business operations could be adversely affected.

The response to the COVID-19 pandemic may redirect resources with respect to regulatory and intellectual property matters in a way that would adversely impact our ability to progress regulatory approvals and protect our intellectual property. In addition, we may face impediments to regulatory meetings and in obtaining regulatory approvals due to measures intended to limit in-person interactions which could adversely impact the ability of regulatory authorities to take all steps needed to grant regulatory approval and

could cause regulatory authorities to defer action on our regulatory submissions, including limitations or delays of inspections of facilities by regulatory authorities, which may impact approval timelines.

Any negative impact that the COVID-19 pandemic has on recruiting or retaining patients in our clinical trials or on the ability of our suppliers to provide materials for our product candidates could cause additional delays to clinical trial activities, which could materially and adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, affect our ability to raise additional capital, and have a material adverse effect on our financial results.

The COVID-19 pandemic has significantly impacted economies worldwide, which could result in adverse effects on our business and operations. We cannot be certain what the overall impact of the continuation or worsening of the COVID-19 pandemic may be on our business. It has the potential to adversely affect our business, financial condition, results of operations, and prospects.

We are dependent on the success of EMPAVELI and the successful development and commercialization of pegcetacoplan in other jurisdictions and disease indications. If we are unable to successfully commercialize EMPAVELI or develop, obtain marketing approval for or successfully commercialize systemic pegcetacoplan in other indications, either alone or through a collaboration, or if we experience significant delays in doing so, our business could be harmed.

We are investing a significant portion of our efforts and financial resources to fund the commercialization of EMPAVELI and development of systemic pegcetacoplan in other disease indications. Our prospects are dependent on our ability to successfully commercialize EMPAVELI in the United States. We are also dependent on the success of pegcetacoplan in clinical development and our ability to obtain additional marketing approvals for pegcetacoplan in one or more other indications. Pursuant to our agreement with Sobi, we have granted to Sobi the exclusive right to commercialize systemic pegcetacoplan outside the United States. Our prospects are substantially dependent on our ability, or that of Sobi or any future collaborator, to successfully commercialize EMPAVELI and to develop, obtain marketing approval for and successfully commercialize pegcetacoplan in additional disease indications. All of our other product candidates are in early stages of clinical development.

The success of EMPAVELI in PNH and pegcetacoplan in other disease indications will depend on several factors, including the following:

- our ability to successfully commercialize of EMPAVELI in the United States, including establishing sales, marketing and distribution capabilities for EMPAVELI;
- commercial acceptance by patients, the medical community and third-party payors of EMPAVELI in PNH, pegcetacoplan in other indications, if approved, and other product candidates, if approved;
- 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, including approval of EMPAVELI from the EMA;
- 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;
- obtaining pegcetacoplan drug product from third-party manufacturers of sufficient quality to be used in our clinical trials and for commercial sale;
- developing, validating and maintaining a commercially viable manufacturing process that is compliant with current good manufacturing practices, or cGMPs;
- the performance of Sobi and any future collaborators;

- 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;
- a continued acceptable safety profile following any marketing approval;
- 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 our collaborators, including Sobi. If we are unable to successfully commercialize EMPAVELI in the United States for PNH or to develop, receive marketing approval for and successfully commercialize pegcetacoplan in other indications on our own or with a 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, may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.

We 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 received an approval for EMPAVELI for the treatment of patients with PNH in the United States and Saudi Arabia, and an approval for Aspaveli in the EU and Australia, but there is no assurance that we will receive regulatory approvals for pegcetacoplan for the treatment of PNH in other jurisdictions, for GA in any jurisdiction, or for other indications in any jurisdiction. We 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 additional 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 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.

We plan to submit a new drug application, or NDA, to the FDA in the second quarter of 2022 for the approval of intravitreal pegcetacoplan for the treatment of geographic atrophy, or GA, which submission would be supported by the completed Phase 2 and Phase 3 clinical trials of intravitreal pegcetacoplan in patients with GA. Any delay in submitting the NDA, or adverse action by the FDA, could delay our planned commercial development timelines or could prevent us from commercializing intravitreal pegcetacoplan. If the FDA determines that our NDA and the data supporting the NDA are not sufficient to support approval in GA, we may be required to conduct an additional clinical trial, which would increase our costs and delay the program. Any such delay or other adverse impact could have a material adverse effect on our business.

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 ophthalmological 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 modified our manufacturing process in order to eliminate an impurity in the active pharmaceutical ingredient 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, and we announced that we completed enrollment in July 2020.

In March 2021, we decided not to pursue additional development of APL-9 for the treatment of severe COVID-19. The decision followed an interim review of mortality data from the Phase 1/2 study by an independent data monitoring committee, or the DMC, which found no meaningful reduction in the overall mortality rate in patients treated with APL-9 in combination with standard of care therapy compared to standard of care alone. No safety signals were observed by the DMC.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us and impair our ability to generate revenues from product sales, regulatory and commercialization milestones, and royalties. Moreover, if we are required to conduct additional clinical trials or other testing of our product candidates beyond the trials and testing that we contemplate, if we 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 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.

Under our collaboration with Sobi, we are relying on Sobi to conduct certain clinical trials of systemic pegcetacoplan and seek regulatory approval for systemic pegcetacoplan outside the United States. If Sobi or any future collaborator are unable to successfully complete clinical trials of our product candidates and obtain regulatory approvals on a timely basis, or at all, our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties may be materially impaired.

In addition, investigators for our clinical trials and other service providers 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, or any collaborator conducting clinical trials of our product candidates such as Sobi, 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 our Phase 2 trials 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.

In our Phase 3 trials of pegcetacoplan in patients with GA, the most frequently reported adverse events were associated with the injection procedure in the study eye. During the 12-month treatment period and the subsequent six-month period during which no treatment was administered, we observed that 6.0% of patients who received administration of pegcetacoplan every month and 4.1% of patients who received administration of pegcetacoplan every other month showed new onset exudation in the study eye as compared to 2.4% of the sham group.

In 2018, during the early part of 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 intravitreal pegcetacoplan 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.

If any of our product candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, we, or our collaborators, may 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 we, or any collaborator conducting clinical trials of any of our product candidates such as Sobi, 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 our 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 our 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 our collaborators, anticipate, patient enrollment in these clinical trials may be slower than we, or our collaborators, anticipate or participants may drop out of these clinical trials at a higher rate than we, or our 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 our collaborators, including those manufacturing our product candidates or components or ingredients thereof or conducting clinical trials on our behalf or on behalf of our collaborators, may deviate from the trial protocol, fail to comply with regulatory requirements or fail to meet their contractual obligations to us or our collaborators in a timely manner or at all;
- regulators or institutional review boards may not authorize us, our collaborators or our or their investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we, or our 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 our 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 our 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 our collaborators', clinical trial designs or our or their interpretation of data from preclinical studies and clinical trials;
- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third-party manufacturers with which we, or our 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.

Should the COVID-19 pandemic persist, our clinical development plans could be affected, and we may be unable to conduct our clinical trials in the manner or on the timelines that we currently anticipate. Clinical trial participants and clinical investigators may not be able to comply with clinical trial protocols, if for example quarantines or other travel limitations impede participant movement, affect sponsor access to study sites, or interrupt healthcare services. The COVID-19 pandemic could lead to delayed enrollment in our trials, more frequent missed appointments and withdrawals from ongoing trials and more frequent or severe adverse events during our trials. In particular, we believe that COVID-19 may have impacted enrollment in certain of our clinical studies, including the Phase 2 MERIDIAN study that we are conducting in patients with ALS.

Product development costs for us will increase if we experience delays in testing or pursuing marketing approvals and we 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 our collaborators, may have the exclusive right to commercialize our product candidates or allow our competitors, or the competitors of our collaborators, to bring products to market before we, or our collaborators, do and impair our ability, or the ability of our 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 collaborator conducting clinical trials of any of our product candidates such as Sobi, 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 our 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.

Many of the indications for which we are developing product candidates are rare diseases with small patient populations, 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. These difficulties may be exacerbated as a result of the ongoing COVID-19 pandemic.

Our inability, or the inability of our 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 our 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.

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 our 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.

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. 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 obtained marketing approval for only one product and we may be unable to obtain, or may be delayed in obtaining, marketing approval for any of our product candidates.

We have obtained marketing approval for only one product, EMPAVELI, which the FDA approved in May 2021 for the treatment of patients with PNH, and which the EC approved as Aspaveli in December 2021 for the treatment of patients with PNH who are anemic after treatment with a C5 inhibitor for at least three months. In the future, with respect to NDAs or MAAs for pegcetacoplan for other indications or product candidates, if the FDA or EMA does not accept or approve such NDAs or MAAs, 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 required trials or studies, approval of any

NDA, MAA 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 or EMA to approve our NDAs or MAAs.

Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing pegcetacoplan in the United States or EU for PNH or for other indications, generating revenues and achieving and sustaining profitability. If any of these outcomes occur, either to pegcetacoplan or to any future product candidate for which we may seek marketing approval, we may be forced to abandon or limit our development efforts for pegcetacoplan or such future product candidates, which could significantly harm our business.

Even if pegcetacoplan or one of our other product candidates that we develop 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 our 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 our collaborators, 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 that may be observed once the product has been commercialized. If safety problems occur or are identified after EMPAVELI or intravitreal pegcetacoplan or one of our products, if any, 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, 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 our 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 our collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or our 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.

We 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, of any products for which we obtain marketing approval, including EMPAVELI, in which case we may not generate significant revenues or become profitable.

We may fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success of any products for which we obtain marketing approval, including EMPAVELI. 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 though we have obtained marketing approval of EMPAVELI, we may not be able to successfully convince physicians or patients to switch from eculizumab or ravulizumab to pegcetacoplan. In addition, even though switching from eculizumab and ravulizumab is expressly contemplated in the label for EMPAVELI for the treatment of PNH, 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 products and product candidates may require significant resources and may not be successful. If EMPAVELI or any of our product candidates for which we obtain marketing approval do 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 EMPAVELI or our other product candidates for which we obtain marketing approval, 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;
- the price at which the product is offered for sale;
- 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.

In addition, the potential market opportunity for EMPAVELI in PNH or in any other indication is difficult to precisely estimate. Our estimates of the potential market opportunity for EMPAVELI in PNH or in other indications include several key assumptions based on our industry knowledge, industry publications, third-party research reports and other surveys. However, no independent source has verified such assumptions. If any of these assumptions proves to be inaccurate, then the actual market for EMPAVELI in PNH or any other indication could be smaller than our estimates of potential market opportunity. If the actual market for EMPAVELI in PNH in other indications is smaller than we expect, our product revenue may be limited, and it may be more difficult for us to achieve or maintain profitability.

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 the commercial launch of EMPAVELI in the United States for PNH for which we recruited a sales force and established marketing, market access and medical affairs teams and distribution capabilities is not successful for any reason, we could incur substantial costs and our investment would be lost if we cannot retain or reposition our sales, marketing, market access and medical affairs personnel.

To achieve commercial success for EMPAVELI, we have expended and anticipate that we will continue to expend significant resources to support our sales force, marketing, market access and medical affairs teams and distribution capabilities. There are risks

involved with establishing our own sales, marketing, distribution, training and support capabilities. For example, recruiting and training sales and marketing personnel is expensive and time consuming and could delay our ability to focus on other priorities. If the commercial launch of EMPAVELI is not successful for any reason, this would be costly, and our investment would be lost if we cannot retain or reposition our sales, marketing, market access and medical affairs personnel or terminate on favorable terms any agreements entered into with third parties to support our commercialization efforts.

Factors that may inhibit our efforts to commercialize EMPAVELI on our own in the United States include:

- our inability to train and retain adequate numbers of effective sales, marketing, training and support personnel;
- the inability of sales personnel to obtain access to physicians, including key opinion leaders, or to educate an adequate number of physicians of
- the benefits of EMPAVELI over alternative treatment options;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with
- more extensive or integrated product offerings; and
- unforeseen costs and expenses associated with establishing and maintaining an independent sales, marketing, training and support organization.

If our salesforce, marketing, market access and medical affairs teams and distribution capabilities fail, or are otherwise unsuccessful, it would materially adversely impact the commercial launch of EMPAVELI, impact our ability to generate revenue and harm our business.

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 EMPAVELI, pegcetacoplan in other indications or any of our other product candidates for which we obtain marketing approval.

We are building sales, marketing and distribution infrastructure in the United States to support commercialization of EMPAVELI and are currently developing additional infrastructure for our other product candidates, including intravitreal pegcetacoplan as a treatment for GA.

We are building focused capabilities to commercialize EMPAVELI in PNH and other indications where we believe that the medical specialists for such 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. 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 EMPAVELI or our other product candidates that receive marketing approval.

We have granted exclusive commercialization rights for systemic pegcetacoplan outside of the United States to Sobi under our agreement with Sobi. If Sobi is unable to meet its contractual obligations, we may be forced to focus our efforts internally to commercialize systemic pegcetacoplan outside of the United States without the assistance of a commercialization partner or seek another commercialization partner, either of which would result in us incurring greater expenses and could cause a delay in market penetration while we expand our commercial operations or seek an alternative commercialization partner. Such costs may exceed the increased revenues we would receive from direct systemic pegcetacoplan sales outside of the United States, at least in the near term.

We would also be forced to declare a breach of the agreement with Sobi and seek a termination of the agreement which could result in an extended and uncertain dispute with Sobi, including arbitration or litigation, any of which would be costly.

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, as described in "Business - Competition," above. We face significant competition with respect to EMPAVELI. We expect that we, and our 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 our 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.

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 EMPAVELI or any product candidates that we are currently developing or that we may develop, which could render EMPAVELI or our product candidates obsolete and noncompetitive.

EMPAVELI targets a market that is already served by a competitor with significantly greater financial resources than us. The principal competitors for EMPAVELI for the treatment of PNH, are eculizumab (marketed as Soliris) and ravulizumab (marketed as Ultomiris), C5 inhibitors developed and marketed by Alexion AstraZeneca Rare Disease, or AstraZeneca. Prior to the approval of EMPAVELI, eculizumab and ravulizumab were the only drugs approved for the treatment of PNH. These products have widespread acceptance among clinicians, patients and payors. Eculizumab and ravulizumab may also compete with EMPAVELI in other indications in our hematology and nephrology programs. AstraZeneca is also developing a subcutaneous version of ravulizumab, currently in phase 3 clinical trial.

We are also aware of several other companies that are actively developing product candidates using complement inhibition for the treatment of PNH in late-stage clinical development, and that there are a number of companies that are actively developing product candidates for the treatment of GA.

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 our collaborators, may develop. Our competitors also may obtain FDA or other marketing approval for their products before we, or our collaborators, are able to obtain approval for ours, which could result in our competitors establishing a strong market position before we, or our 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 an ANDA 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.

EMPAVELI or any product candidate that we or any collaborator, such as Sobi, commercialize 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 EMPAVELI or any our product candidates that we or any collaborator, such as Sobi, commercialize 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 our collaborators, may not be able to successfully commercialize EMPAVELI or any other product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or our 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 our 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 our 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 our collaborators, to commercialize EMPAVELI or 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 our collaborators to sell EMPAVELI or 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 our 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 our 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, or any collaborator that is commercializing our product candidates such as Sobi are unable to obtain coverage or reimbursement for our products, as monotherapy or in combination with other therapies, including possible combinations with eculizumab or ravulizumab, at the levels anticipated, our financial condition could be harmed. Additionally, if new compounds currently in development by potential competitors, including biosimilars of eculizumab or ravulizumab, 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, such as EMPAVELI and coverage may be more limited for EMPAVELI than the indication 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 collaborator, including Sobi, 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 our 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 EMPAVELI and any other products that we may develop.

We face an inherent risk of product liability claims as a result of the commercial sale of EMPAVELI and the clinical testing of our product candidates despite obtaining appropriate informed consents from our clinical trial participants. 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 EMPAVELI and any other product candidates 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 successfully commercialize EMPAVELI or any other 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 EMPAVELI and any other product candidate 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 EMPAVELI and our other 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. In addition, these contractors may be adversely affected by the COVID-19 pandemic. 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 commercial supply for EMPAVELI and clinical supply for our product candidates 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 pegcetacoplan or our other 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 also rely upon contract manufacturers, and potentially collaboration partners to manufacture commercial quantities of EMPAVELI and any of our other product candidates, if approved. We may be unable to establish any agreements with contract manufacturers or to do so on acceptable terms, or to maintain such agreements as we may enter. 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 EMPAVELI or 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. In particular, we have entered into commercial supply agreements with Bachem and NOF to purchase a significant portion of our requirements for the pegcetacoplan drug substance and drug intermediaries, respectively, over the next five years. We have also entered into long-term commercial supply agreements with other suppliers of raw materials, drug intermediaries, drug substance and drug product. 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 clinical trials in patients with GA and wet AMD due to observed cases of non-infectious inflammation in patients treated from a single manufacturing lot of pegcetacoplan ophthalmological 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 for us or our collaborators. Accordingly, for example, if Bachem or NOF were to experience manufacturing and supply issues, we would have difficulty in procuring the drug substance or drug intermediates needed for the supply and manufacture of pegcetacoplan. Additionally, we rely on third parties to supply the raw materials needed to manufacture our product candidates. 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. If we or any third-party parties on which we rely are adversely impacted by restrictions or limitations resulting from the COVID-19 pandemic, our ability to manufacture and supply pegcetacoplan may be disrupted, which would limit our ability to conduct our clinical trials or prepare for our commercial launch. 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.

For EMPAVELI and any product candidates that are approved by any regulatory agency, we will need to maintain 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 are using one or more commercially available ambulatory infusion pumps in our ongoing and planned clinical trials and for our commercial launch of EMPAVELI. 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 EMPAVELI or our product candidates may harm our future profit margins and our ability to commercialize EMPAVELI or any other products that receive marketing approval on a timely and competitive basis.

Our prospects for the development and commercialization of our product candidates will depend in significant part on the success of our collaboration with Sobi and future collaborations.

We have entered into a collaboration with Sobi for the global co-development and commercialization outside of the United States of systemic pegcetacoplan and we may seek to enter into additional collaborations for the development and commercialization of certain of our product candidates. We may have limited control over the amount and timing of resources that our collaborators, including Sobi, will dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, our 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.

For example, our agreement with Sobi is subject to early termination in the event of any uncured material breach of the agreement or under specific circumstances relating to insolvency. If we do not maintain a productive collaborative relationship with Sobi or if Sobi is unable to meet its contractual obligations or if there is an early termination of the agreement as described above, we would be forced to either establish a commercial infrastructure outside of the United States so that we could undertake the commercialization efforts which had been theretofore undertaken by Sobi or we would need to seek an alternative collaborator. The establishment of a commercial infrastructure and assumption by us of commercialization activities outside of the United States would require substantial resources, financial and otherwise, and could result in us incurring greater expenses than the increase in revenues from our direct sales of systemic pegcetacoplan. It could also cause a delay in market penetration while we expand our commercial operations. Seeking and obtaining an alternative collaborator outside the United States could also adversely impact sales of systemic pegcetacoplan and market penetration outside of the United States.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If our collaborators, including Sobi are 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.

We have in the past established, and in the future, may seek to establish, additional 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 entered into the collaboration agreement with Sobi in October 2020 concerning the development and commercialization of pegcetacoplan and specified other structurally and functionally similar compstatin analogues or derivatives for use systemically or for local non-ophthalmic administration. We may seek to establish one or more additional 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. In our collaboration agreement with Sobi, we agreed not to, directly or indirectly, alone or with or for any other person or entity, conduct any clinical development or commercialization of APL-9 for PNH, cold agglutinin disease, hematopoietic stem cell transplantation thrombotic microangiopathy, C3 glomerulopathy and immune complex membranoproliferative glomerulonephritis, and amyotrophic lateral sclerosis or any other indications subsequently agreed upon by the parties.

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.

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 The University of Pennsylvania 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 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 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 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 issue 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 products 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 products or 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 products or product candidates or their methods of use or our approach to complement inhibition, we may not be free to manufacture or market our products or 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 or 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 products or 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 products or 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 products and 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. The "march-in" provisions of the Bayh-Dole Act allow, the U.S. government under strictly 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. Penn has requested a waiver of the U.S. manufacturing requirement, but there can be no assurance that such waiver will be granted.

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 products or 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. For instance, under the Sobi collaboration, we retain the primary right to prosecute and defend its patent and other intellectual property rights, but Sobi has the primary right to enforce such rights against competitive infringement outside the United States.

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 our products or product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of our products or 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, 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 products and 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 products or 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 or 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

The regulatory approval process is expensive, time consuming and uncertain and may prevent us or our collaborators such as Sobi from obtaining approvals for the commercialization of pegcetacoplan or any of our product candidates that we develop. As a result, we cannot predict when or if, and in which territories, we, or our collaborators, will obtain marketing approval to commercialize pegcetacoplan or any other product candidate that we develop.

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 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. The FDA approved EMPAVELI in May 2021 and the EMA granted approval in December 2021. 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, including manufacturing information, to regulatory authorities for each therapeutic indication to establish the product candidate’s safety and efficacy. 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 our 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.

Finally, disruptions at the FDA and other agencies may prolong the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Should the FDA determine that an inspection is necessary for approval of a regulatory submission and an inspection cannot be completed during the review cycle due to restrictions on travel due to COVID-19, and the FDA does not determine a remote interactive evaluation to be adequate, the FDA has stated that it generally intends to issue a complete response letter or defer action on the regulatory submission until an inspection can be completed.

Under our agreement with Sobi, Sobi is responsible for seeking regulatory approval outside the United States for systemic pegcetacoplan. A delay in obtaining or failure to obtain required approvals and clearances could negatively impact our ability or that of our collaborators, including Sobi, 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 EMPAVELI, pegcetacoplan in other indications or any of our other products in the European Union and other foreign jurisdictions, we, and our collaborators, such as Sobi, 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 our collaborators, such as Sobi, 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, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the recent withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. On December 24, 2020, the United Kingdom and the European Union entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction, and the United Kingdom and EU continue to work on the rules for implementation. Since the regulatory framework for pharmaceutical products in the United Kingdom covering the 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, would prevent us from commercializing any product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability, which could significantly and materially harm our business.

We, or our 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 our collaborators, may seek orphan drug designations for pegcetacoplan for other indications and for other product candidates and may be unable to obtain such designations.

Even if we, or our 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 our 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.

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 and/or priority review designation by the FDA or PRIME designation in the EU for one or more of our product candidates may not actually lead to a faster development or regulatory review or approval process, nor does it assure approval of the product candidate by the FDA or the EMA.

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.

Further, if the FDA determines that a product candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or thereafter.

The FDA has broad discretion on whether to grant fast track designation and/or priority review designation to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Even if our product candidates receive fast track designation and/or priority review designation, we may not experience a faster development process, review or approval, if at all, compared to conventional FDA procedures.

In addition, in the EU, we may seek PRIME designation for one or more of our product candidates. The program focuses on product candidates that target conditions for which there exists no satisfactory method of treatment in the EU or product candidates that may offer a major therapeutic advantage over existing treatments. The benefits of a PRIME designation include, among other things, the potential to qualify product for accelerated review, meaning reduction in the review time for an opinion on approvability to be issued earlier in the application process. PRIME designation enables an applicant to request parallel EMA scientific advice and health technology assessment advice to facilitate timely market access. Even if our product candidates receive PRIME designation, we may not experience a faster development process, review or approval compared to conventional EMA procedures and it does not assure or increase the likelihood of the EMA's grant of a marketing authorization.

Even if we, or our 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 our collaborators, must therefore comply with requirements concerning advertising and promotion for any of our product candidates which we or they market. 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 our collaborators will not be able to promote any products we develop for indications or uses for which they are not approved. We are limited to promoting EMPAVELI in accordance with its approved label in each jurisdiction and may not

promote it for any indication other than PNH. The label in the European Union is more limited than the label for EMPAVELI in the United States.

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, our collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, given the marketing approval of EMPAVELI and assuming we, or our collaborators, receive marketing approval for one or more of our other product candidates, we, and our 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 our collaborators, are not able to comply with post-approval regulatory requirements, we, and our collaborators, could have the marketing approvals for our products withdrawn by regulatory authorities and our, or our 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.

EMPAVELI and any other product candidates for which we, or our collaborators, obtain marketing approval in the future could be subject to post-marketing restrictions or withdrawal from the market and we, or our 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.

EMPAVELI and any other product candidates for which we, or our 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. For EMPAVELI and any other product candidate that is granted marketing approval, 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 our 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.

Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Separately, in response to the COVID-19 pandemic, since March 2020, when foreign and domestic inspections of facilities were largely placed on hold, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. The FDA has developed a rating system to assist in determining when and where it is safest to conduct prioritized domestic inspections. As of May 2021, certain inspections, such as foreign pre-approval, surveillance, and for-cause inspections that are not deemed mission-critical, remain temporarily postponed. In April 2021, the FDA issued guidance formally announcing plans to employ remote interactive evaluations, using risk management methods, to meet user fee commitments and goal dates and in May 2021 announced plans to continue progress toward resuming standard operational levels. Should the FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be adequate, the FDA has stated that it generally intends to issue a complete response letter or defer action on the application until an inspection can be completed.

In 2020 and 2021, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. As of May 2021, the FDA noted it was continuing to ensure timely reviews of applications for medical products during the ongoing COVID-19 pandemic in line with its user fee performance goals and conducting mission-critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. However, the FDA may not be able to continue its current pace and review timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the ongoing COVID-19 pandemic and travel restrictions, the FDA is unable to complete such required inspections during the review period. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

Current and future legislation may increase the difficulty and cost for us and our collaborators to obtain reimbursement 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 our collaborators, to profitably sell EMPAVELI or any other 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 our collaborators, may receive for any approved products. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed.

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. This legislation resulted in aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031. However, pursuant to the CARES Act and subsequent legislation, these Medicare sequester reductions are suspended through the end of March 2022 and from April 2022 through June 2022, a 1% cut will be in effect, with the full 2% cut resuming thereafter. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several 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.

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. A ruling by the Court is expected sometime this year. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden revoked these orders and issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access This Executive Order also directs the U.S. Department of Health and Human Services to create a special enrollment period for the Health Insurance Marketplace in response to the COVID-19 pandemic. We cannot predict how federal agencies will respond to such Executive Orders.

Further, outside of the US, including the countries of the EU, 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 drug. To obtain reimbursement or pricing approval in some countries, we, or our collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our products 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 materially harmed.

The prices of prescription pharmaceuticals in the United States and foreign jurisdictions are subject to considerable legislative and executive actions and could impact the prices we obtain for our products, if and when approved.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, there have been several recent U.S. congressional inquiries, as well as 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 products. To those ends, the Trump Administration issued several executive orders intended to lower the costs of prescription drug products. Certain of these orders are reflected in recently promulgated regulations, including an interim final rule implementing the Trump Administration's most favored nation model, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries effective, but such final rule is currently subject to a nationwide preliminary injunction. In addition, on August 21, 2021, CMS issued a new proposed rule to rescind President Trump's interim final rule, following public notice and comment, and CMS stated it will explore all options to incorporate value into payments for Medicare Part B drugs and improve beneficiaries' access to evidence-based care.

The Biden Administration has frozen certain of the Trump administration's measures to reform drug prices. It remains to be seen how the Biden Administration will address this issue but, under Medicare Part D, the new administration may seek to establish a ceiling for the launch prices of all branded, biologic, and certain generic drugs by referencing the average price of these drugs in other developed countries. At the same time, the administration may seek to limit Medicare Part D and public option drug prices through a tax penalty on manufacturers for increases in the cost of drugs and biologics above the general inflation rate. The American Rescue Plan Act of 2021, comprehensive COVID-19 relief legislation recently enacted under the Biden Administration, includes a number of healthcare-related provisions, such as support to rural health care providers, increased tax subsidies for health insurance purchased through insurance exchange marketplaces, financial incentives to states to expand Medicaid programs and elimination of the Medicaid drug rebate cap effective in 2024.

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 organizations 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.

In countries outside of the United States, particularly 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 may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate 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, possibly materially.

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.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, imprisonment and the curtailment or restructuring of our operations, any of which could adversely affect our business, financial condition, results of operations and prospects.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the European Union. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of European Union Member States, such as the UK Bribery Act 2010. Violation of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union Member States.

These requirements are provided in the national laws, industry codes or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

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. Liabilities they incur pursuant to these laws could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

With the passage of the CREATES Act, we are exposed to possible litigation and damages by competitors who may claim that we are not providing sufficient quantities of our approved products on commercially reasonable, market-based terms for testing in support of their ANDAs and 505(b)(2) applications.

In December 2019, former President Trump signed legislation intended to facilitate the development of generic and biosimilar products. The bill, previously known as the CREATES Act, authorizes sponsors of abbreviated new drug applications, or ANDAs, and 505(b)(2) applications to file lawsuits against companies holding NDAs that decline to provide sufficient quantities of an approved reference drug on commercially reasonable, market-based terms. Drug products on FDA's drug shortage list are exempt from these new provisions unless the product has been on the list for more than six continuous months or the FDA determines that the supply of the product will help alleviate or prevent a shortage.

To bring an action under the statute, an ANDA or 505(b)(2) applicant must take certain steps to request the reference product, which, in the case of products covered by a Risk Evaluation and Mitigation Strategy with elements to assure safe use, include obtaining authorization from the FDA for the acquisition of the reference product. If the applicant does bring an action for failure to provide a reference product, there are certain affirmative defenses available to the NDA holder, which must be shown by a preponderance of evidence. If the applicant prevails in litigation, it is entitled to a court order directing the NDA holder to provide, without delay, sufficient quantities of the applicable product on commercially reasonable, market-based terms, plus reasonable attorney fees and costs.

Additionally, the new statutory provisions authorize a federal court to award the product developer an amount "sufficient to deter" the NDA holder from refusing to provide sufficient product quantities on commercially reasonable, market-based terms if the court finds, by a preponderance of the evidence, that the NDA holder did not have a legitimate business justification to delay providing the product or failed to comply with the court's order. For the purposes of the statute, the term "commercially reasonable,

market-based terms" is defined as (1) the nondiscriminatory price at or below the most recent wholesale acquisition cost for the product, (2) a delivery schedule that meets the statutorily defined timetable, and (3) no additional conditions on the sale.

Although we intend to comply fully with the terms of these new statutory provisions, we are still exposed to potential litigation and damages by competitors who may claim that we are not providing sufficient quantities of our approved products on commercially reasonable, market-based terms for testing in support of ANDAs and 505(b)(2) applications. Such litigation would subject us to additional litigation costs, damages and reputational harm, which could lead to lower revenues. The CREATES Act may enable generic competition with EMPAVELI and any of our product candidates, if approved, which could impact our ability to maximize product revenue.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the EU General Data Protection Regulation, or the GDPR, which took effect across all member states of the European Economic Area, or EEA, in May 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 increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater, and it 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. In addition, the GDPR provides that European Union member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

Similar actions are either in place or under way in the United States. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act—which went into effect on January 1, 2020—is creating similar risks and obligations as those created by GDPR, though the Act does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with these requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

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 us 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. The FCPA is enforced by the DOJ and the SEC.

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, hospital clinics, universities and similar institutions are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials, regulatory approvals, sales and marketing and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions. Because the FCPA applies to indirect payments, the use of third parties and other collaborators can increase potential FCPA risk, as we could be held liable for the acts of third parties that do not comply with the FCPA's requirements.

The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

Like the FCPA, the UK Bribery Act and other anti-corruption laws throughout the world similarly prohibit offers and payments made to obtain improper business advantages, including offers or payments to healthcare professionals and other government and non-government officials. These other anti-corruption laws also can result in substantial financial penalties and other collateral consequences.

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.

We are subject to governmental export and import controls that could impair our or our collaborators' ability to compete in international markets due to licensing requirements and subject us or them to liability if we or they are not in compliance with applicable laws.

Our products are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls. Exports of our products outside of the U.S. must be made in compliance with these laws and regulations. If we or our collaborators fail to comply with these laws and regulations, we or they and certain of our or their employees could be subject to substantial civil or criminal penalties, including the possible loss of export or import privileges; fines, which may be imposed on us or our collaborators and the respective responsible employees or managers; and, in extreme cases, the incarceration of responsible employees or managers.

In addition, changes in our products or changes in applicable export or import laws and regulations may create delays in the introduction, provision, or sale of our products in international markets, prevent customers from using our products or, in some cases, prevent the export or import of our products to certain countries, governments or persons altogether. Any limitation on our ability to export, provide, or sell our products could adversely affect our business, financial condition and results of operations.

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.

Our employees or consultants 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 of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee or consultant 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. This could include violations of HIPAA, other U.S. federal and state law, and requirements of non-U.S. jurisdictions, including the European Union Data Protection Directive. It is not always possible to identify and deter employee or consultant 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, regulations, guidance or codes of conduct. 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 fines or other sanctions.

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 Scientific Officer. The members of our executive team are employed "at will," meaning any of them may terminate his or her 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.

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 2021, the number of our employees increased from 374 on December 31, 2020 to 476 on December 31, 2021. We expect the number of employees to continue to increase in 2022. Our principal office is located in Massachusetts and we maintain additional offices in California, Australia 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 temporarily closed our facilities in March 2020 in response to the COVID-19 pandemic. We have since re-opened our physical facilities on a limited basis, subject to compliance with strict safety guidelines, but most of our employees continue to work remotely. In the event of a renewal of shelter-in-place orders or and mandated local travel restrictions, our employees conducting research and development activities may not be able to access our facilities and our activities may be significantly limited or curtailed, possibly for an extended period of time. Furthermore, it is possible that over the long term our operational efficiency may be decreased if our employees and third-party collaborators are unable to meet and work in the same physical location.

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. These risks may be particularly acute given the rapid growth in the size of our company. 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 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:

- our success in launching and commercializing EMPAVELI and, if approved, intravitreal pegcetacoplan;
- 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;
- the effect of the COVID-19 outbreak on the healthcare system and the economy generally and on our clinical trials and other operations specifically;
- 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, cash equivalents and marketable securities 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 is required to devote substantial time to compliance initiatives and corporate governance practices.

As a public company, we incur significant legal, accounting and other expenses. 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. Our management and other personnel devote and will need to continue to devote, a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly.

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.

We have registered all shares of common stock that we may issue under our equity compensation plans. As of December 31, 2021, we had options to purchase an aggregate of 12,561,532 shares of our common stock outstanding, of which options to purchase 7,698,532 shares were vested and 1,228,406 outstanding unvested restricted stock units that upon vesting would result in the issuance of 1,228,406 shares of our common stock. 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 10,778,303 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.

Changes in tax laws or in their interpretation could adversely affect our business and financial condition.

Recent changes in tax law could adversely affect our business or financial condition. On December 22, 2017, the U.S. government enacted 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, or the Code. The TCJA, among other things, contained 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 for losses arising in taxable years ending after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), 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.

As part of Congress' response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, was enacted on March 18, 2020, and the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, was enacted on March 27, 2020. COVID relief provisions were also included in the Consolidated Appropriations Act, 2021, or CAA, which was enacted on December 27, 2020. The FFCR Act, the CARES Act, and the CAA contain numerous tax provisions. In particular, the CARES Act retroactively and temporarily (for taxable years beginning before January 1, 2021) suspends application of the 80%-of-income limitation on the use of net operating losses, which was enacted as part of the TCJA. It also provides that net operating losses arising in any taxable year beginning after December 31, 2017, and before January 1, 2021, are generally eligible to be carried back up to five years. The CARES Act also temporarily (for taxable years beginning in 2019 or 2020) relaxes the limitation on the tax deductibility of net interest expense by increasing the limitation from 30% to 50% of adjusted taxable income.

Regulatory guidance under the TCJA, the FFCR Act, the CARES Act, and the CAA is and continues to be forthcoming, and such guidance could ultimately increase or lessen the impact of these laws on our business and financial condition. Congress may enact additional legislation in connection with the COVID-19 pandemic, some of which could have an impact on our company. In addition, it is uncertain if and to what extent various states will conform to the TCJA, the FFCR Act, the CARES Act, or the CAA.

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, 2021, we had both federal and state net operating loss carryforwards of $355.8 million and $411.2 million, respectively, and federal and state research and development tax credit carryforwards of $54.2 million and $11.4 million, respectively. Federal net operating loss carryforward generated post-2017 in the amount of $276.9 million may be carried forward indefinitely. The remaining net operating loss and research and development tax credit carryforwards will begin to expire in 2033. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the TCJA, as modified by the CARES act, 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 in 2021 and future years is limited. Certain states have also enacted temporary suspension or limitation of the utilization of net operating loss carryforwards. In addition, under Section 382 of the Code, 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. Refer to Note 15, "Income Taxes," of the consolidated financial statements included in this Annual Report on Form 10-K for additional information related to our accounting for income taxes.

Taxing authorities could challenge our historical and future tax positions or our allocation of taxable income among our subsidiaries, and tax laws to which we are subject could change in a manner adverse to us.

We operate through various subsidiaries in a number of countries throughout the world. Consequently, we are subject to tax laws, treaties, and regulations in the countries in which we operate, and these laws and treaties are subject to interpretation. We have taken, and will continue to take, tax positions based on our interpretation of such tax laws. Our transfer pricing arrangements are not generally binding on applicable tax authorities. The price charged for products, services, or the royalty rates and other amounts paid for intellectual property rights, could be challenged by the various tax authorities, resulting in additional tax liability, interest, and/or penalties. There can be no assurance that a taxing authority will not have a different interpretation of applicable law and assess us with additional taxes. If we are assessed with additional taxes, this may result in a material adverse effect on our results of operations and/or financial condition.

Any changes to existing accounting pronouncements or taxation rules or practices may cause adverse fluctuations in our reported results of operations or affect how we conduct our business.

A change in accounting pronouncements or taxation rules or practices can have a significant effect on our reported results and may affect our reporting of transactions completed before the change is effective. New accounting pronouncements, taxation rules and varying interpretations of accounting pronouncements or taxation rules have occurred in the past and may occur in the future. The change to existing rules, future changes, if any, or the need for us to modify a current tax or accounting position may adversely affect our reported financial results or the way we conduct our business.

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 executive officers and directors, entities associated with our executive officers and directors and our largest stockholders may allow these stockholders to significantly influence matters submitted to our stockholders for approval, as well as our management and affairs.

As of February 23, 2022, our executive officers and directors, and entities associated or affiliated with our executive officers and directors, in the aggregate, beneficially owned shares representing approximately 21.3% of our outstanding common stock, including our largest stockholder, Morningside Venture Investments, Ltd., which beneficially owned approximately 12.9% 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 will not apply to actions arising under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended. 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 77,818 square feet in Waltham, Massachusetts under a lease that expires in December 2026, office space of approximately 9,478 square feet in San Francisco, California under a lease that expires in April 2024; office space of approximately 938 square meters in Zug, Switzerland under a lease that expires in July 2025; lab space of approximately 9,704 square feet in Watertown, Massachusetts under a lease that expires in August 2027; and office space of approximately 241 square meters in Melbourne, Australia under a lease that expires in January 2024. Our lease for 7,125 square feet of office space in Crestwood, Kentucky terminated in January 2021.

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 23, 2022, we had 19 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, 2021, 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.

Item 6. Reserved

Not applicable.

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 commercial-stage biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutic compounds to treat diseases with high unmet needs 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.

In May 2021, the U.S. Food and Drug Administration, or the FDA, approved EMPAVELI (pegcetacoplan), the first targeted C3 therapy and our first approved product, for the treatment of paroxysmal nocturnal hemoglobinuria, or PNH. EMPAVELI is approved for use in adults with PNH and can be used by patients who are either treatment-naïve or who are switching from C5 inhibitors eculizumab or ravulizumab. We believe that EMPAVELI has the potential to elevate the standard of care in PNH and are seeking to establish EMPAVELI as the preferred first-line treatment for patients. In the United States, there are approximately 1,500 patients with PNH currently being treated with C5 inhibitors and another 150 patients who are expected to be newly diagnosed each year. Between our launch of EMPAVELI in May 2021 through December 31, 2021, we generated $15.1 million in net product revenue from sales of EMPAVELI.

In December 2021, the European Commission, or the EC, approved Aspaveli (pegcetacoplan) for the treatment of adults with PNH who are anemic after treatment with a C5 inhibitor for at least three months. In January 2022, systemic pegcetacoplan was also approved for the treatment of PNH in Saudi Arabia and Australia. Systemic pegcetacoplan is currently marketed under the trade name EMPAVELI™ in the United States, Saudi Arabia and Australia and Aspaveli® in the European Union. Under our collaboration and license agreement with Swedish Orphan Biovitrum AB (Publ), or Sobi, Sobi has global co-development and exclusive ex-U.S. commercialization rights for systemic pegcetacoplan and intends to initiate the commercial launch of Aspaveli in jurisdictions outside of the United States during the first quarter of 2022. We have commercialization rights for systemic pegcetacoplan in the United States.

We also are leveraging our expertise in targeting C3 to advance intravitreal pegcetacoplan as the first potential treatment for geographic atrophy, or GA, secondary to age-related macular degeneration, or AMD. Intravitreal pegcetacoplan has the potential to be a breakthrough for patients with GA, a disease that affects approximately one million people in the U.S. and five million people worldwide. Based on the results of our Phase 3 (DERBY and OAKS) and Phase 2 (FILLY) clinical trials of intravitreal pegcetacoplan, we intend to submit a new drug application, or NDA, to the FDA in the second quarter of 2022 with a request for six-month priority review. We also plan to submit a market authorization application, or MAA, to the European Medicines Agency, or the EMA, in the second half of 2022. We have exclusive, worldwide commercialization rights for intravitreal pegcetacoplan.

We believe that inhibition of the complement system by targeting C3 may enable a broad range of therapeutic approaches, and that pegcetacoplan has the potential to address the limitations of existing treatment options or provide a treatment option in indications where there currently are none. Under our collaboration with Sobi, we are co-developing systemic pegcetacoplan for cold agglutinin disease, or CAD, and hematopoietic stem cell transplantation-associated thrombotic microangiopathy, or HSCT-TMA, in hematology; C3 glomerulopathy, or C3G, and immune complex membranoproliferative glomerulonephritis, or IC-MPGN, in nephrology; and amyotrophic lateral sclerosis, or ALS, in neurology.

We are also evaluating the administration of systemic pegcetacoplan as an approach to enabling adeno-associated virus, or AAV, vector administration for gene therapies. We believe complement inhibition may yield three important benefits when used in combination with AAV-delivered gene therapies: increasing the safety of AAV-delivered gene therapies, decreasing the required AAV dose needed to achieve a therapeutic effect, and allowing for dosing in patients who have pre-existing antibodies. In collaboration with commercial and academic researchers, we are advancing pre-clinical studies to assess the impact of complement inhibition on AAV-delivered gene therapies and expect to report pre-clinical data in the first half of 2022.

Lastly, we are developing other product candidates with other routes of administration and plan to conduct clinical trials of these product candidates, including the combination of EMPAVELI and a small interfering RNA, or siRNA, which may offer the potential to reduce the treatment frequency of EMPAVELI by reducing the production of C3 proteins in the liver. Furthermore, we are

collaborating with Beam Therapeutics, Inc., or Beam, on up to six research programs focused on C3 and other complement targets in the eye, liver and brain, using Beam's proprietary base editing technology to discover new treatments for complement-driven diseases.

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 and executing the commercial launch of our products and providing general and administrative support for these operations.

To date, we have financed our operations primarily through $1.2 billion in net proceeds from public offerings of our common stock, including our initial public offering, or IPO, $535.8 million in net proceeds from the private offerings of Convertible Notes, a $250.0 million upfront payment and $25.0 million as development reimbursement payments from Sobi each pursuant to the Sobi collaboration agreement, $112.6 million in proceeds from the private placement of shares of our convertible preferred stock prior to our IPO, $140.0 million under 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. We have repaid the term loan facility and the promissory note in full. We exchanged $327.2 million of aggregate principal amount of 2019 Convertible Notes for shares of our common stock during 2021. During the quarter ended September 30, 2021, the Convertible Notes were convertible at the option of the holders, and certain holders of the Convertible Notes converted approximately $0.7 million of aggregate principal amount of Convertible Notes into an aggregate of 18,775 shares. The shares were issued in October 2021.

Since the launch of EMPAVELI in May 2021 through December 31, 2021, we generated $15.1 million of net product revenue from sales of EMPAVELI. We have incurred significant annual net operating losses in each year since our inception and expect to continue to incur net operating losses for at least this year and next year. Our net losses were $746.4 million, $344.9 million and $304.7 million for the years ended December 31, 2021, 2020 and 2019, respectively. As of December 31, 2021, we had an accumulated deficit of $1.7 billion. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase significantly particularly as we continue to incur significant commercialization expenses related to building sales, marketing, medical affairs, manufacturing, distribution and other commercial infrastructure associated with the commercialization of EMPAVELI for the treatment of PNH. We are incurring significant expenses for the commercialization and further development of intravitreal pegcetacoplan. In addition, we expect our expenses to increase if and as we continue to develop and conduct our ongoing and planned clinical trials of pegcetacoplan and our other product candidates; 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 to commercialize any additional 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, regulatory and scientific personnel; add operational, financial and management information systems and personnel, including personnel to support our product development and add equipment and physical infrastructure to support our research and development programs and commercialization.

As of December 31, 2021, we had cash, cash equivalents and marketable securities of $700.6 million. We believe that our cash and cash equivalents and marketable securities, along with cash anticipated to be generated from sales of EMPAVELI and the first regulatory milestone payment and committed development reimbursement payments from Sobi, as of December 31, 2021, will be sufficient to enable us to fund our current operations at least into the second quarter of 2023. 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."

We temporarily closed our facilities in March 2020 in respect to the COVID-19 pandemic. We have since reopened our facilities on a limited basis, subject to compliance with strict safety guidelines, but most of our employees continue to work remotely. We do not believe that the COVID-19 pandemic has had a significant impact upon our operations, including sales of EMPAVELI, our ongoing clinical trials (except for the delay of the clinical trials in patients with ALS) and the manufacture and supply of our product candidates.

SFJ Agreement

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 systemic 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.

On June 7, 2019, we amended 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 systemic pegcetacoplan for the treatment of patients with PNH.

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.

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 and in January 2020 received the remaining $20.0 million installment of the additional $60.0 million upon the announcement of the results of the PEGASUS phase 3 trial.

Under the SFJ agreement, following regulatory approvals by the FDA and the EMA for the use of systemic pegcetacoplan as a treatment for PNH, we paid SFJ initial payments of $4.0 million in 2021 and $5.0 million in 2022, respectively, and we are obligated to pay SFJ an additional $451.0 million in the aggregate in six additional annual payments with the majority of the payments being made from the third anniversary to the sixth anniversary of regulatory approval.

Convertible Notes

In September 2019, we issued and sold $220.0 million aggregate principal amount of 3.5% convertible senior notes due 2026, or the 2019 Convertible Notes, in a private offering. The net proceeds from the sale of the 2019 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 offering to pay the cost of the capped call transactions in September 2019 described below.

In May 2020, we issued and sold an additional $300.0 million aggregate principal amount of 3.5% convertible senior notes due 2026, or the 2020 Convertible Notes, in a private offering. The aggregate purchase price of the 2020 Convertible Notes was $328.9 million, which amount included accrued interest from March 15, 2020 to, but not including, May 12, 2020. The net proceeds from the sale of the 2020 Convertible Notes were approximately $322.9 million after deducting the initial purchasers' discounts and commissions and offering expenses payable by us. We used $43.1 million of the net proceeds from the offering to pay the cost of the capped call transactions in May 2020 described below. The 2020 Convertible Notes were issued as additional notes under the Indenture and form a single series with, and have the same terms as, the 2019 Convertible Notes, but have a different issue date, issue price, CUSIP number and different restrictions on transfer. We refer to the 2019 Convertible Notes and the 2020 Convertible Notes together as the Convertible Notes.

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 $39.4625 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 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 governing the Convertible Notes, or the Indenture.

Prior to March 15, 2026, the Convertible Notes are convertible only under the following circumstances:

- during any calendar quarter, if the last reported sale price of our common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on, and including, the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day;
- during the five business day period after any five consecutive trading day period in which the trading price per $1,000 principal amount of the Convertible Notes for each such trading day was less than 98% of the product of the last reported sale price of our common stock and the conversion rate on each such trading day;
- if we call any or all of the Convertible Notes for redemption, at any time prior to the close of business on the second scheduled trading day immediately preceding the redemption date; or
- upon the occurrence of corporate events specified in the Indenture.

On and 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.

In January 2021, we entered into separate, privately negotiated exchange agreements with certain holders of our 2019 Convertible Notes. Under the terms of these exchange agreements, the holders exchanged approximately $126.1 million in aggregate principal amount of 2019 Convertible Notes held by them for an aggregate of 3,906,869 shares of our common stock. The exchange transactions closed in January 2021. We also issued 69,491 shares for settlement of issuance costs paid to our financial advisor for services performed in connection with the exchanges.

In July 2021, we entered into separate, privately negotiated exchange agreements to modify the conversion terms with certain holders of the 2020 Convertible Notes. Under the terms of these exchange agreements, the holders exchanged approximately $201.1 million in aggregate principal amount of 2019 Convertible Notes and 2020 Convertible Notes held by them for an aggregate of 5,992,217 shares of common stock. The exchange transactions closed in July 2021. We also issued 78,419 shares for settlement of issuance costs paid to our financial advisor for services performed in connection with the exchanges.

During the quarter ended September 30, 2021, the Convertible Notes were convertible at the option of the holders, and certain holders of the Convertible Notes converted approximately $0.7 million of aggregate principal amount of Convertible Notes into an aggregate of 18,775 shares. The shares were issued in October 2021.

Capped Call Transactions

In September 2019 and May 2020, concurrently with the pricing of the 2019 Convertible Notes and 2020 Convertible Notes, respectively, 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, 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.

Collaboration Agreement with Sobi

On October 27, 2020, we entered into the collaboration agreement with Sobi, concerning the development and commercialization of pegcetacoplan and specified other structurally and functionally similar compstatin analogues or derivatives for use systemically or for local non-ophthalmological administration, collectively referred to as the licensed products. See "Business—Collaboration and License Agreement with Sobi" for a description of the key terms of our collaboration agreement with Sobi. We granted Sobi an exclusive (subject to certain rights retained by us), sublicensable license of certain patent rights and know-how to develop and commercialize licensed products in all countries outside of the United States. We retained the right to commercialize licensed products in the United States, and, subject to specified limitations, to develop licensed products worldwide for commercialization in the United States. Under the agreement, Sobi made an upfront payment of $250.0 million in November 2020, and agreed to pay up to an aggregate of $915.0 million upon the achievement of specified one-time regulatory and commercial milestone events, including a $50.0 million milestone which would be payable following the first regulatory and reimbursement approval of systemic pegcetacoplan in any major European country, and to reimburse us for up to $80.0 million in development costs. In January 2021 we received a $25.0 million development reimbursement payment from Sobi and in January 2022 we received a $20.0 million development reimbursement payment. We expect to receive the balance annually in installments over the next two years, subject to certain conditions.

European Commission approval of systemic pegcetacoplan for the treatment of PNH was received in December 2021. If systemic pegcetacoplan receives reimbursement approval in any major European country, Sobi will be required to make a milestone payment of $50.0 million to us. We considered the reimbursement approval to be probable at December 31, 2021, and have recorded revenue for the milestone payment of $50.0 million. We expect to fully achieve the milestone and receive payment from Sobi in the first half of 2022. We are also entitled to receive tiered, double-digit royalties (ranging from high teens to high twenties) on sales of licensed products outside of the United States, subject to customary deductions and third-party payment obligations, until the latest to occur of: (i) expiration of the last-to-expire of specified licensed patent rights; (ii) expiration of regulatory exclusivity; and (iii) ten (10) years after the first commercial sale of the applicable licensed product, in each case on a licensed product-by-licensed product and country-by-country basis. We remain responsible for our license fee obligations (including royalty obligations) to the University of Pennsylvania and for our payment obligations to SFJ Pharmaceuticals.

Financial Operations Overview

Revenue

We have not generated significant revenue from product sales. As a result of the commercial launch of EMPAVELI in the United States in May 2021, we commenced sales of EMPAVELI in May 2021. Our revenues consist of product sales of EMPAVELI and revenues derived from our collaboration arrangement with Sobi. See Note 13, License and Collaboration Agreements, included in Item 15 in this Annual Report on Form 10-K, for more information related to the Sobi Collaboration and License Agreement.

We account for contracts with our customers in accordance with Revenue from Contracts with Customers (Topic 606). Pursuant to ASC 606, for arrangements or transactions between arrangement participants determined to be within the scope of the contracts with customers guidance, we perform the following five steps to determine the appropriate amount of revenue to be recognized as we fulfil our obligations: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) we satisfy each performance obligation.

Revenue is recognized when, or as, we satisfy a performance obligation by transferring a promised good or service to a customer. An asset is transferred when, or as, the customer obtains control of that asset. For performance obligations that are satisfied over time, we recognize revenue using an input or output measure of progress that best depicts the satisfaction of the relevant performance obligation.

Product Revenues

For the year ended December 31, 2021, our revenues from net product sales were generated in the United States following the FDA's approval for marketing of EMPAVELI for the treatment of PNH in May 2021. We sell EMPAVELI principally through arrangements with specialty pharmacies, or SPs, and specialty distributors, or SDs, who are our customers. The customers subsequently resell the product to patients and health care providers. We apply the ASC 606 five step process discussed above to the contracts with SPs and SDs. We provide limited right of return to the customers in cases of shipping error or product defect, including inactive or non-moving products due to market conditions. Product revenues are recognized when the customers take control of the product, which typically occurs upon delivery to the customers.

We recognize revenue from product sales at the net sales price which includes estimates of variable consideration for which reserves are established and reflects each of these as a reduction to the revenue. Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the contract. The amount of variable consideration that is included in the transaction price may be constrained. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from estimates, we may need to adjust our estimates, which would affect net revenue in the period of adjustment. The following are our significant categories of sales discounts and allowances:

Distribution Fees: Distribution fees include distribution service fees paid to SPs and SDs based on a contractually fixed percentage of the wholesale acquisition cost (WAC), fees for data, and prompt payment discounts. We do not receive a distinct good or service in exchange for the payment. Distribution fees are recorded as an offset to revenue based on contractual terms at the time revenue from the sale is recognized.

Chargebacks: Chargebacks are discounts and fees related to contracts with various third-party payers including pharmacy benefit managers, private healthcare insurers and government healthcare programs that purchase from SDs at a discounted price. SDs charge back to us the difference between the price initially paid by SDs and the discounted price paid to SDs by these entities. We issue credit notes for the chargeback which are applied to future sales.

Product Returns: Consistent with industry practice, we offer SPs and SDs limited product return rights for damages, shipment errors, and expiring or defective products; provided that the return is within a specified period around the product expiration date as set forth in the applicable individual distribution agreement. We do not allow product returns for product that has been dispensed to a patient. As we receive inventory reports from SPs and SDs, we have visibility into the inventory distribution channel, enabling us to make a reasonable estimate of future potential product returns based on this on-hand channel inventory data and sell-through data obtained from SPs and SDs. In arriving at our estimate for product returns we also consider historical product returns (to the extent available), the underlying product demand, and industry data specific to the specialty pharmaceutical distribution industry.

Licensing and Collaboration Revenue

We enter into licensing agreements from time to time in which we receive upfront payments, milestone payments and royalties. In 2020 we entered into a collaboration agreement with Sobi for the development and commercialization of systemic pegcetacoplan, described below, and two license agreements with third parties to use APL-9 in certain research projects.

We analyze our license and collaboration arrangements pursuant to FASB ASC Topic 808, Collaborative Arrangement Guidance and Considerations to assess whether such arrangements, or transactions between arrangement participants, involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities or are more akin to a vendor-customer relationship. In making this evaluation, we consider whether the activities of the collaboration are considered to be distinct and deemed to be within the scope of the collaborative arrangement guidance and those that are more reflective of a vendor-customer relationship and, therefore, within the scope of the revenue with contracts with customers guidance. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement.

For elements of collaboration arrangements that are not accounted for pursuant to the revenue from contracts with customers guidance, an appropriate recognition method is determined and applied consistently, generally by analogy to the revenue from contracts with customers guidance. Amounts related to transactions with a counterparty in a collaborative arrangement that is not a customer are presented as collaboration revenue and on a separate line item from revenue recognized from contracts with customers, if any, in our consolidated statements of operations.

We recognize revenue when a customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, Revenue from Contracts with Customers (“ASC 606”), the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract, determines those that are performance obligations and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Pursuant to ASC 606, we recorded the $250.0 million non-refundable upfront payment in revenue for the year ended December 31, 2020, as the payment was associated with the transfer of the good or services in the form of the license to Sobi. The $80.0 million reimbursement for research and development activities does not constitute a customer/vendor relationship and thus is not in the scope of ASC 606. As ASC 808 does not include recognition guidance, we established an accounting policy to recognize the payments under the reimbursement as a receivable on the balance sheet in an amount that is probable to be reimbursed based upon expense incurred by us, with a contra-research and development expense recognized in the statement of operations. See Note 13, License and Collaboration Agreements, included in Item 15 in this Annual Report on Form 10-K, for more information related to the Sobi Collaboration and License Agreement.

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 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 costs of operating as a public company.

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.

Product Revenues

As of December 31, 2021, our revenues from net product sales were generated in the United States following the FDA's approval for marketing of EMPAVELI for the treatment of PNH in May 2021. We sell EMPAVELI principally through arrangements with SPs and SDs who are our customers. The customers subsequently resell the product to patients and health care providers.

We account for contracts with its customers in accordance with ASC 606. Pursuant to ASC 606, for arrangements or transactions between arrangement participants determined to be within the scope of the contracts with customers guidance, we perform the following five steps to determine the appropriate amount of revenue to be recognized as we fulfill our obligations: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) we satisfy each performance obligation.

Revenue is recognized when, or as, we satisfy a performance obligation by transferring a promised good or service to a customer. An asset is transferred when, or as, the customer obtains control of that asset. For performance obligations that are satisfied over time, we recognize revenue using an input or output measure of progress that best depicts the satisfaction of the relevant performance obligation.

We recognize revenue from product sales at the net sales price which includes estimates of variable consideration for which reserves are established and reflects each of these as a reduction to the revenue. Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the contract. The amount of variable consideration that is included in the transaction price may be constrained. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from estimates, we may need to adjust its estimates, which would affect net revenue in the period of adjustment. The following are our significant categories of sales discounts and allowances:

Distribution Fees: Distribution fees include distribution service fees paid to SPs and SDs based on a contractually fixed percentage of the wholesale acquisition cost (WAC), fees for data, and prompt payment discounts. We do not receive a distinct good or service in exchange for the payment.

Distribution fees are recorded as an offset to revenue based on contractual terms at the time revenue from the sale is recognized.

Chargebacks: Chargebacks are discounts and fees relate to contracts with various third-party payers including pharmacy benefit managers, private healthcare insurers and government healthcare programs that purchase from SDs at a discounted price. SDs charge back to us the difference between the price initially paid by SDs and the discounted price paid to SDs by these entities. We issue credit notes for the chargeback which are applied to future sales.

Product Returns: Consistent with industry practice, we offer SPs and SDs limited product return rights for damages, shipment errors, and expiring product; provided that the return is within a specified period around the product expiration date as set forth in the applicable individual distribution agreement. We do not allow product returns for product that has been dispensed to a patient. As we receive inventory reports from SPs and SDs and has visibility into the inventory distribution channel, it is able to make a reasonable estimate of future potential product returns based on this on-hand channel inventory data and sell-through data obtained from SPs and SDs. In arriving at our estimate for product returns, we also consider historical product returns, the underlying product demand, and industry data specific to the specialty pharmaceutical distribution industry.

Licensing Revenue

On October 27, 2020, we entered into the collaboration agreement with Sobi concerning the development and commercialization of pegcetacoplan and specified other compstatin analogues or derivatives for use systemically or for local non-ophthalmic administration, collectively referred to as the Licensed Products. See "Business—Collaboration and License Agreement with Sobi" for a description of the key terms of our collaboration agreement with Sobi.

We have determined that the collaboration agreement is within the scope of FASB ASC Topic 808, *Collaborative Arrangements* ("ASC 808") as a contractual arrangement that involves a joint operating activity whereby both parties are (i) active participants in the activity and (ii) exposed to certain significant risks and rewards dependent on the commercial success of the activity. ASC Topic 808 does not address measurement or recognition matters but allows for analogizing to ASC 606, *Revenue from Contracts with Customers*

("ASC 606"). Pursuant to ASC 606, we performed the following five steps: (i) identified the contract with a customer; (ii) identified the performance obligations in the contract; (iii) determined the transaction price; (iv) allocated the transaction price to the performance obligations in the contract; and (v) recognized revenue when the entity satisfied a performance obligation.

We identified the following material promises under the Sobi Agreement: (1) licenses to develop and commercialize pegcetacoplan, or Licenses to IP, and (2) performance of research and development services. We determined the promises to be distinct because Sobi can benefit from each of the license and the development services on their own or with readily available services. We could have provided the license without any development services and Sobi would have been able to benefit from it by obtaining development services from another provider as the Licensed Products are at a more mature stage in their life cycle.

Under the collaboration agreement, Sobi agreed to pay us:

i) a fixed amount of $250.0 million in an upfront payment in November 2020;
ii) a fixed amount of an additional $80.0 million in development reimbursements, payable yearly in four tranches in amounts determined based upon actual expenses incurred by us;
iii) up to an aggregate of $915.0 million upon the achievement of specified one-time regulatory and commercial milestone events; and
iv) tiered, double-digit royalties, ranging from high teens to high twenties, on sales of Licensed Products outside of the United States, subject to customary deductions and third-party payment obligations.

At inception of the collaboration agreement, we considered the $250.0 million non-refundable payment and the $80.0 million fixed proceeds. We also evaluated whether Sobi is a customer for either of the distinct promises in the agreement. Under the Licenses to IP, we determined that Sobi is a customer as the know-how provided and the rights granted by us to Sobi are outputs of our business activities for which we will receive consideration. With respect to research and development activity, management determined that there is no vendor relationship as performing research and development activities for others is not a part of our ongoing central operations. Based upon the evaluation of the relative fair values, we allocated the purchase price of $250.0 million and the related milestones and royalties to the license of IP and $80.0 million to performance of research and development activities.

The milestone and royalty payments are subject to activities outside our control. Per ASC 606, we consider this to be a customer/ vendor relationship; therefore, we will include the regulatory milestone payments in the total transaction price when it is probable that a significant reversal of revenue would not occur in a future period. We will recognize commercial milestone and royalty revenue at the later of (i) when the related sales occur or (ii) when the performance obligation to which the commercial milestone or royalty has been allocated has been satisfied. In case of commercial milestone or royalty payments, we will recognize revenue in the same period that the sales are completed for which we are contractually entitled to the milestone or percentage-based royalty payment. To date, we have not recognized any commercial milestone or royalty revenue resulting from any of our licensing arrangements. Management will periodically assess the elements of the contract and re-evaluate revenue recognition as necessary.

Pursuant to ASC 606, the $250.0 million non-refundable upfront payment is recognized as revenue as this is the amount allocated to the license. The $80.0 million reimbursement for research and development activities does not constitute a customer/vendor relationship and, thus, is not in the scope of ASC 606. As ASC 808 does not include recognition guidance we have established an accounting policy to recognize the payments under the reimbursement as a receivable on the balance sheet in an amount that is to be reimbursed based upon expense incurred by us, with a contra- research and development expense recognized in the statement of operations, over time as the expenses are incurred. See Note 13, License and Collaboration Agreements, included in Item 15 in this Annual Report on Form 10-K, for more information related to the Sobi Collaboration and License Agreement.

Cost of Research Collaboration Arrangement

We analyze research collaboration arrangements pursuant to ASC 808 to assess whether such arrangements, or transactions between arrangement participants, involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. If each party is actively participating in this activity and exposed to significant risks and rewards related to the activity, each party's costs will be accounted for under ASC 808.

Since ASC 808 does not provide recognition guidance, we refer to the guidance under ASC 730 to arrangements involving our payments to third parties. ASC 730 requires us to recognize research and developments costs as expense as incurred since there is no alternative use. See Note 13, License and Collaboration Agreements, in the Notes to Consolidated Financial Statements included in Item 15 in this Annual Report on Form 10-K for more information.

Inventory

Inventory is recorded at the lower of cost or net realizable value, with cost determined on a first-in, first-out basis. Inventory costs include third-party contract manufacturing, third-party packaging services, and freight. We primarily use actual costs to determine the cost basis for our inventory. We periodically review our inventories to identify obsolete, slow moving, excess or otherwise unsaleable items. The determination of whether inventory costs will be realizable requires estimates by management. We did not have any obsolete inventory as of December 31, 2021.

Prior to regulatory approval of our product candidates, we expense costs associated with the manufacture of our product candidates to research and development expense unless we are reasonably certain such costs have future commercial use and net realizable value. When we believe regulatory approval and subsequent commercialization of our product candidates is probable, and we also expect future economic benefit from the sales of the product candidates to be realized, we will then capitalize the costs of production as inventory.

Prior to receiving FDA approval for EMPAVELI on May 14, 2021, we included in research and development expense the costs associated with the manufacture of EMPAVELI inventory to be sold upon commercialization. As a result, the manufacturing costs related to the EMPAVELI inventory build-up incurred before FDA approval were already expensed in a prior period and are therefore excluded from the cost of goods sold as of December 31, 2021.

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.

Convertible Notes

On September 16, 2019, we completed a private offering of the 2019 Convertible Notes with an aggregate principal amount of $220.0 million. On May 12, 2020, we issued the 2020 Convertible Notes with an aggregate principal amount of $300.0 million.

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 the 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 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.

Effective January 1, 2021, we early adopted ASU 2020-06, *Debt – Debt with Conversion and Other Options (Subtopic 470-20)* which reduces complexity in applying GAAP to certain financial instruments with characteristics of liability and equity. The ASU removes the guidance that requires entities to account for beneficial conversion features and cash conversion features in equity, separately from the host convertible debt or preferred stock. The ASU further revises the guidance to require entities to calculate diluted earnings per share for convertible instruments by using the if-converted method. In addition, we must presume share settlement for purposes of calculating diluted earnings per share when an instrument may be settled in cash or shares. The impact of the adoption

of the statement increased net debt outstanding and decreased net equity by $149.7 million as of January 1, 2021. Of the $149.7 million decrease to net equity, $16.0 million was recorded to retained earnings.

In January 2021, we entered into separate, privately negotiated exchange agreements with certain holders of the 2019 Convertible Notes. Under the terms of these exchange agreements, the holders exchanged approximately $126.1 million in aggregate principal amount of 2019 Convertible Notes held by them for an aggregate of 3,906,869 shares of common stock. The exchange transactions closed in January 2021. We also issued 69,491 shares for settlement of issuance costs paid to our financial advisor for services performed in connection with the exchanges.

In July 2021, we entered into separate, privately negotiated exchange agreements to modify the conversion terms with certain holders of the 2020 Convertible Notes. Under the terms of these exchange agreements, the holders exchanged approximately $201.1 million in aggregate principal amount of 2019 Convertible Notes and 2020 Convertible Notes held by them for an aggregate of 5,992,217 shares of common stock. The exchange transactions closed in July 2021. We also issued 78,419 shares for settlement of issuance costs paid to our financial advisor for services performed in connection with the exchanges.

In September 2021, the Convertible Notes were convertible at the option of the holders, and certain holders of the Convertible Notes converted approximately $0.7 million of aggregate principal amount of Convertible Notes into an aggregate of 18,775 shares. The shares were issued in October 2021.

As of the date of this Annual Report on Form 10-K, we hold the $327.2 million principal of exchanged notes and such notes have not been cancelled. Approximately $192.0 million is outstanding and held by third parties as of December 31, 2021.

Capped Call Transactions

On September 11, 2019, and May 6, 2020, concurrently with the pricing of the 2019 Convertible Notes and 2020 Convertible Notes, respectively, 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 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, 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 premiums paid in the amount of $43.1 million was recorded as a reduction to additional paid-in capital as of December 31, 2020 for the Convertible Notes. See Note 8, Long-term Debt, included in Item 15 in this Annual Report on Form 10-K, for more information related to the capped call transactions.

Development Derivative Liability and Development Liability

Prior to obtaining Regulatory Approval, we presented the SFJ agreement as a derivative liability, which was recorded at fair value and remeasured each quarter with the change in fair value recognized in earnings.

The SFJ agreement was presented as a derivative liability on the consolidated balance sheet as of December 31, 2020. 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 the years ended December 31, 2020 and 2019, we received an additional $20.0 million and $60.0 million, respectively, as we met certain milestones. The SFJ agreement was remeasured quarterly as a level 3 derivative, with the total change in fair value for the years ended December 31, 2020 and 2019 of $103.0 million and $14.8 million, respectively, recorded in loss from remeasurement of development derivative liability on the consolidated income statement.

The derivative was valued using a scenario-based discounted cash flow method, whereby each scenario made assumptions about the probability and timing of cash flows, and such cash flows are present valued using a risk-adjusted discount rate. The analysis was 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 included (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 (12.65%).

SFJ's implied cost of borrowing was 8.0% and our implied cost of borrowing was 12.65% as of December 31, 2020. 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.

On May 14, 2021, we obtained regulatory approval of EMPAVELI in the United States from the FDA. On December 15, 2021, we obtained regulatory approval in the European Union from the EMA. Following the FDA and EMA approvals, we have a fixed payment schedule to pay SFJ the initial payment and subsequent annual payments as outlined in the SFJ agreement.

Prior to the EMA approval, the SFJ agreement was presented as a derivative liability on the consolidated balance sheet and, as such, was recorded at fair value and remeasured each quarter. The total change in fair value of $97.7 million and $103.0 million were recorded for the years ended December 31, 2021 and 2020, respectively, in loss from remeasurement of development derivative liability in the consolidated statements of operations and comprehensive loss. The remeasurement of the development derivative liability resulted in a remeasured fair value of $257.9 million as of December 31, 2020 on the consolidated balance sheet. At December 31, 2020, $4.2 million of the $257.9 million of the development derivative liability fair market value was included in current liabilities.

Following the EMA approval, we are obligated to make payments following pre-determined fixed payment schedules as set forth in the SFJ agreement and SFJ amendment to pay SFJ the initial and subsequent annual payments totaling $456.0 million as of December 31, 2021 (excluding the $4.0 million initial payment for FDA approval made in June 2021) with the initial payment for EMA approval of $5.0 million due January 2022, which we paid in January 2022, and final annual payment due December 2027. As the variability of the future payments derived from the underlying contingency (i.e., EMA approval and FDA approval) no longer exist, we remeasured the development derivative liability on December 15, 2021 and reclassified it from development derivative liability to development liability, with subsequent accounting to follow an effective interest accretion schedule to the fixed payment amounts. For the year ended December 31, 2021, the loss from remeasurement of the development derivative liability was recorded through December 15, 2021, when it was determined that the SFJ agreement was no longer a derivative.

From December 15, 2021 and thereafter until the final annual payment is due in December 2027, the development liability will be accreted from its initial carrying amount to the total payment amount using the effective interest rate method under ASC 835 over the remaining life of the SFJ agreement. The difference between the carrying amount and the total payment amount is presented as discount to the development liability. The accretion is recorded as interest expense in the consolidated income statement.

Results of Operations

Comparison of Years Ended December 31, 2021 and 2020

The following table summarizes our results of operations for the years ended December 31, 2021 and 2020, together with the dollar increase or decrease and percentage change in those items:

(in thousands)	Year Ended December 31, 2021	Year Ended December 31, 2020	Change $	Change %
Revenue:				
Product Revenue, net	$ 15,147	$ —	15,147	100%
Licensing and other revenue	51,416	250,646	(199,230)	(79)
Total revenue:	66,563	250,646	(184,083)	(73)
Operating expenses:				
Cost of sales	200	—	200	100
Research and development	345,869	299,921	45,948	15
Cost of research collaboration	75,000	—	75,000	100
License expense	5,000	25,050	(20,050)	(80)
General and administrative	176,771	139,401	37,370	27
Total operating expenses	602,840	464,372	138,468	30
Net operating loss	(536,277)	(213,726)	(322,551)	151
Loss on conversion of debt	(100,589)	—	(100,589)	100
Loss from remeasurement of development derivative liability	(97,675)	(103,029)	5,354	(5)
Interest income	418	4,164	(3,746)	(90)
Interest expense	(13,241)	(29,937)	16,696	(56)
Other income/(expense), net	1,362	(501)	1,863	(372)
Net loss before taxes	(746,002)	(343,029)	(402,973)	117
Income tax expense	352	1,845	(1,493)	(81)
Net loss	$ (746,354)	$ (344,874)	$ (401,480)	116

Product Revenue, Net

We recognized $15.1 million of net product revenue for the year ended December 31, 2021 from sales of EMPAVELI in the United States. EMPAVELI was approved by the FDA in May 2021, and therefore we did not have any net product revenue for the year ended December 31, 2020.

Licensing and Other Revenue

Licensing revenue decreased $199.2 million for the year ended December 31, 2021 as compared to the year ended December 31, 2020. The decrease is primarily due to the Collaboration and Licensing Agreement we entered with Sobi. Sobi paid us an upfront payment of $250.0 million in November 2020, which we recognized in licensing revenue in the consolidated statement of operations for the year ended December 31, 2020. During the year ended December 31, 2021, we recorded $50.0 million in licensing revenue related to the probable achievement of the development milestone for first regulatory and reimbursement approval in Europe. Licensing and other revenue also includes $1.4 million in revenue for product supplied to Sobi during the year ended December 31, 2021. During the year ended December 31, 2020, we entered into two different licensing and collaboration agreements with third parties to provide APL-9 for use in certain research projects which resulted in licensing revenue of $0.6 million.

Research and Development Expenses

The following table summarizes our research and development expenses incurred during the years ended December 31, 2021 and 2020, together with the dollar increase or decrease and percentage change in those items:

(In thousands)	Year Ended December 31, 2021	Year Ended December 31, 2020	Change $	Change %
Contract manufacturing	$ 68,242	$ 112,820	$ (44,578)	(40%)
Clinical trial costs	121,685	102,243	19,442	19
Compensation and related personnel costs	107,679	76,318	31,361	41
Other development costs	51,625	30,092	21,533	72
Sobi development milestone	(32,026)	(42,975)	10,949	(25)
Research/innovation	18,269	16,382	1,887	12
Pre-clinical study expenses	10,021	4,407	5,614	127
Device development expenses	374	634	(260)	(41)
Research and development expense	345,869	299,921	45,948	15
Cost of research collaboration	75,000	—	75,000	100
License expense	5,000	25,050	(20,050)	(80)
Total research and development expenses including cost of research collaboration and license expense	$ 425,869	$ 324,971	$ 100,898	31

Research and development expenses increased by $100.9 million to $425.9 million for the year ended December 31, 2021 from $325.0 million for the year ended December 31, 2020, an increase of 31%. The increase in research and development expenses was primarily attributable to an increase of $75.0 million in cost of research collaboration attributable to the Beam arrangement, an increase of $31.4 million in compensation and related personnel costs primarily due to the hiring of additional personnel in 2021, an increase of $19.4 million in clinical trial costs associated with the continued enrollment and conduct of our clinical trials in several indications, a decrease of $10.9 million contra research and development expense related to the Sobi transaction, an increase of $1.9 million related to research and innovation costs, an increase of $21.5 million in other research and development supporting activities primarily driven by regulatory, quality and medical affairs expenses, and an increase of $5.6 million in preclinical study expenses. These increases were partially offset by a decrease of $44.6 million in contract manufacturing expenses due primarily to the timing of drug supply and analytical activity as well as the capitalization of inventory following FDA approval of EMPAVELI in May 2021, a decrease of $20.0 million for the licensee fee to Penn related to the Sobi transaction, and a decrease of $0.2 million in device development expenses.

General and Administrative Expenses

General and administrative expenses increased by $37.4 million to $176.8 million for the year ended December 31, 2021, from $139.4 million for the year ended December 31, 2020, an increase of 27%. The increase in general and administrative expenses was attributable to an increase in employee related costs of $26.3 million, an increase in professional and consulting fees and commercial preparation activities of $10.6 million, an increase in insurance costs of $0.1 million, an increase of $2.5 million in director stock option compensation, an increase of $0.8 million in travel, offset by $2.9 million decrease in office costs and other. The increased employee related costs of $26.3 million consisted of $15.8 million related to an increase in salaries and benefits primarily due to the hiring of additional personnel, $12.3 million related to stock expense associated with the grant of stock options and restricted stock units to employees, offset by a $1.8 million decrease in recruitment expense. The increased professional and consulting fees of $10.6 million primarily consisted of an increase in commercial related activity of $10.7 million and a decrease in general consulting fees of $0.1 million.

Loss on Conversion of Debt

In January 2021 and in July 2021, we entered into separate, privately negotiated exchange agreements to modify the conversion terms with certain holders of the Convertible Notes. Under the terms of these exchange agreements, the holders exchanged in January 2021 and July 2021 approximately $126.1 million and $201.1 million, respectively, in aggregate principal amount of Convertible Notes held by them for an aggregate of 3,906,869 shares and 5,992,217 shares, respectively of common stock issued by us. In accordance with ASC 470-20, we accounted for the exchange as an induced conversion based on the short period of time the conversion offer was open and the substantive conversion feature offer. We accounted for the conversion of the debt as an inducement by expensing the fair value of the shares that were issued in excess of the original terms of the Convertible Notes.

For the January 2021 transaction, we reduced net debt outstanding and increased net equity on the consolidated balance sheet by $122.8 million, consisting of the par value of the 2019 Convertible Notes exchanged of $126.1 million less the $3.3 million of

remaining debt issuance costs associated with the exchanged notes. We also increased shares outstanding by 3,906,869 shares consisting of 3,196,172 shares issued at the initial conversion rate in the indenture of 25.3405 plus an additional 710,697 shares. Additionally, we issued 69,491 shares as settlement of debt issuance costs to our financial advisor in connection with the conversion transaction. We recorded a loss on conversion of debt of $39.5 million comprised of $36.4 million related to the value of the shares issued in excess of the original conversion terms at the fair market value and $3.1 million for the value of the 69,491 shares issued in payment of issuance costs. Upon exchange of the 2019 Convertible Notes, the holders forfeited accrued interest through the date of the exchange of $1.7 million, which we charged to interest expense and to equity.

For the July 2021 transaction, we reduced net debt outstanding and increased net equity on the consolidated balance sheet by $197.0 million, consisting of the par value of the Convertible Notes exchanged of $201.1 million less the $4.1 million of remaining debt issuance costs associated with the exchanged notes. We also increased shares outstanding by 5,992,217 shares consisting of 5,097,166 shares issued at the initial conversion rate in the Indenture of 25.3405 plus an additional 895,051 shares. Additionally, we issued 78,419 shares as settlement of debt issuance costs to our financial advisor in connection with the conversion transaction. Upon exchange of the 2019 and 2020 Convertible Notes, the holders forfeited accrued interest through the date of the exchange of $2.5 million, which we charged to interest expense and to equity.

The conditional conversion feature of the Convertible Notes was triggered as of June 30, 2021, and so the Convertible Notes were convertible at the option of the holders until September 31, 2021. Certain holders of the Convertible Notes converted approximately $0.7 million of aggregate principal of Convertible Notes into an aggregate of 18,775 shares. The shares were issued in October 2021.

We recognized $100.6 million of loss on conversion of debt for the year ended December 31, 2021. As of December 31, 2021, we held in treasury Convertible Notes in principal amount of $327.2 million which notes had not been cancelled.

Loss from Remeasurement of Development Derivative Liability

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 development derivative liability was initially recorded at the value of the $60.0 million aggregate cash received pursuant to the contact terms.

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 and in each of September 2019 and January 2020, we achieved a $20.0 million development milestone under the terms of the agreement, resulting in receipt of an aggregate of $60.0 million of additional funding from SFJ.

We remeasured the fair value of the derivative liability as a level 3 derivative at the end of each quarter. The remeasurements resulted in a change in fair value which resulted in a loss of $97.7 million and $103.0 million recorded in the consolidated statement of operations for the years ended December 31, 2021 and 2020, respectively. Prior to the EMA approval of systemic pegcetacoplan on December 15, 2021, the SFJ agreement was presented as a derivative liability on the consolidated balance sheet and, as such, is recorded at fair value and remeasured each quarter. Following the EMA approval obtained on December 15, 2021, we are obligated to make annual payments to SFJ following pre-determined, fixed payment schedules as set forth in the SFJ agreement and SFJ amendment. We made a $4.0 million initial payment to SFJ in June 2021 following FDA approval of systemic pegcetacoplan, and the remaining annual payments due to SFJ totaled $456.0 million as of December 31, 2021, with the initial payment following EMA approval of $5.0 million due in January 2022, which we paid in January 2022, with the final payment due in 2027. As the variability of the future payments derived from the underlying contingency (i.e., EMA approval and FDA approval) no longer exist, we remeasured the development derivative liability on December 15, 2021 and reclassified it from development derivative liability to development liability, with subsequent accounting to follow an effective interest accretion schedule to the fixed payment amounts.

Interest Expense

Interest expense was $13.2 million for the year ended December 31, 2021, a decrease of $16.7 million, compared to $29.9 million for the year ended December 31, 2020. The decrease in interest was primarily due to the decrease in the Convertible Notes outstanding and held by third parties as a result of the exchange transactions as well as the adoption of ASU 2020-06, which reduced the amount of non-cash interest recognized on the debt discount.

Interest Income

Interest income was $0.4 million for the year ended December 31, 2021, a decrease of $3.8 million, compared to $4.2 million for the year ended December 31, 2020. The decrease in interest income was primarily attributable to a decline in investment yields and interest rates.

Other Income, Net

Other Income/(expense) increased $1.8 million for the year ended December 31, 2021 as compared to the year ended December 31, 2020.

Income Tax Expense

Income tax expense decreased $1.5 million for the year ended December 31, 2021 as compared to the year ended December 31, 2020. The decrease was primarily related to foreign income tax expense.

Comparison of the Years Ended December 31, 2020 and 2019

A discussion of changes in our results of operations during the year ended December 31, 2020 compared to the year ended December 31, 2019 has been omitted from this Annual Report on Form 10-K but may be found in "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on February 25, 2021, which discussion is incorporated herein by reference and which is available free of charge on the SECs website at www.sec.gov.

Liquidity and Capital Resources

Sources of Liquidity

To date, we have financed our operations primarily through $1.2 billion in net proceeds from public offerings of our common stock, $535.8 million in net proceeds from offerings of Convertible Notes, a $250.0 million upfront payment and a total of $25.0 million of development reimbursement payments from Sobi pursuant to the Sobi collaboration agreement, $112.6 million in proceeds from the private placement of shares of our convertible preferred stock prior to our IPO, $140.0 million under 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. We have repaid the term loan facility and the promissory note in full, and we exchanged an aggregate of $327.2 million of aggregate principal amount of Convertible Notes for shares of our common stock in January 2021 and July 2021.

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 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.

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 $0.5 million.

On May 12, 2020, we completed a private offering of $300.0 million aggregate principal amount of 2020 Convertible Notes. We received net proceeds of approximately $322.9 million, which included accrued interest March 15, 2020 to, but not including May 12, 2020, and the initial purchasers' discounts and commissions and offering costs of $6.0 million.

On January 6, 2021, we entered into separate, privately negotiated exchange agreements with certain holders of our 2019 Convertible Notes. Under the terms of these exchange agreements, the holders exchanged approximately $126.1 million in aggregate principal amount of 2019 Convertible Notes held by them for an aggregate of 3,906,869 shares of our common stock. These exchange transactions closed in January 2021.

On July 23, 2021, we entered into separate, privately negotiated exchange agreements to modify the conversion terms with certain holders of the 2020 Convertible Notes. Under the terms of these exchange agreements, the holders exchanged approximately

$201.1 million in aggregate principal amount of Convertible Notes held by them for an aggregate of 5,992,217 shares of common stock. These exchange transactions closed in July 2021.

On November 18, 2021, we issued and sold 10,062,500 shares of our common stock in a follow-on offering at a public offering price of $40.00, including 1,312,500 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 $380.4 million after deducting underwriting discounts and commissions of $22.1 million and offering costs of $0.6 million.

In addition to our existing cash, cash equivalents and marketable securities, we anticipate cash to be generated from sales of EMPAVELI and the first regulatory milestone payment and committed development reimbursement payments from Sobi. Our ability to earn these milestone payments and the timing of earning these payments is dependent upon the outcome of our research and development and commercialization activities and is uncertain at this time.

The capped call transactions that we entered into concurrently with the issuance of the Convertible Notes 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.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2021 and 2020:

(in thousands)	**Year Ended December 31,**	
	2021	**2020**
Net cash used in operating activities	$ (563,126)	$ (160,488)
Net cash provided (used in) investing activities	247,616	(316,989)
Net cash provided by financing activities	392,236	692,178
Effect of exchange rate changes on cash and cash equivalents	(2,016)	359
Net increase (decrease) in cash and cash equivalents	$ 74,710	$ 215,060

Net Cash Used in Operating Activities

Net cash used in operating activities was $563.1 million for the year ended December 31, 2021 and consisted primarily of a net loss of $746.4 million adjusted for $276.7 million of non-cash items, including a loss on early exchange of debt of $100.6 million, loss from remeasurement of development derivative liability of $97.7 million and share-based compensation expense of $70.7 million, a net increase in operating assets of $93.6 million, a decrease in accounts payable and accrued expenses of $0.1 million.

Net cash used in operating activities was $160.5 million for the year ended December 31, 2020 and consisted primarily of a net loss of $344.9 million adjusted for $164.8 million of non-cash items, including a loss from remeasurement of development derivative liability of $103.0 million and share-based compensation expense of $45.4 million, a net increase in operating assets of $35.4 million, an increase in accounts payable and accrued expenses of $55.0 million.

Net Cash Provided by (Used in) Investing Activities

Net cash used in investing activities during the year ended December 31, 2021 was $247.6 million due primarily to the purchase of marketable securities.

Net cash used in investing activities during the year ended December 31, 2020 was $317.0 million primarily to the purchase of marketable securities with proceeds from the follow-on common stock offering in January 2020, the issuance of the 2020 Convertible Notes in May 2020 and the $250.0 million from the Sobi agreement offset by the maturities of some of these investments.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $392.2 million during the year ended December 31, 2021 and consisted primarily of proceeds from the follow-on common stock offering in November 2021 of $380.4 million, the receipt of $17.7 million upon the exercise of stock options and the employee share purchase plan, partially offset by $4.0 million for the payment of the development derivative liability as well as $1.8 million for the payment of employee tax withholding related to equity-based compensation.

Net cash provided by financing activities was $692.2 million during the year ended December 31, 2020 and consisted primarily of proceeds from follow-on common stock offering in January 2020 of $381.4 million, the proceeds from the issuance of the 2020

Convertible Notes in May 2020 of $322.9 million, the receipt of $20.0 million from the SFJ agreement and $11.0 million upon the exercise of stock options and the employee share purchase plan, offset by the $43.1 million used to purchase the capped call.

Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution of EMPAVELI and pre-commercialization activities related to pegcetacoplan for GA. In addition, we expect our expenses to increase as we continue the research and development of, and seek marketing approval for, our product candidates. 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 commercialization efforts.

We believe that our cash and cash equivalents and marketable securities as of December 31, 2021, along with cash anticipated to be generated from sales of EMPAVELI and the first regulatory milestone payment and committed development reimbursement payments from Sobi, will enable us to fund our operating expenses and capital expenditure requirements at least into the second quarter of 2023. 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 are devoting resources to the preparation of submission for regulatory approval and to the building of a commercial infrastructure for intravitreal pegcetacoplan for GA. We will incur substantial additional commercialization expenses for intravitreal pegcetacoplan if we obtain marketing approval for GA. We are also devoting additional resources to the development of our other product candidates. We will need to seek additional funding to conduct these activities. Because of the numerous risks and uncertainties associated with the commercialization of EMPAVELI, the development of intravitreal pegcetacoplan and other 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:

- our ability to successfully commercialize and sell EMPAVELI in the United States;
- the cost of and our ability to submit applications for regulatory approval and to build a commercial infrastructure for intravitreal pegcetacoplan for GA in the United States and worldwide;
- the cost of and our ability to effectively establish and maintain, the commercial infrastructure and manufacturing capabilities required to support the commercialization of EMPAVELI, systemic pegcetacoplan and intravitreal pegcetacoplan and any other products for which we receive marketing approval including product sales, medical affairs, marketing, manufacturing and distribution;
- the scope, progress, timing, costs and results of clinical trials of, and research and preclinical development efforts for systemic pegcetacoplan, intravitreal pegcetacoplan and our other product candidates;
- our ability to maintain a productive collaborative relationship with Sobi with respect to systemic pegcetacoplan, including our ability to achieve milestone payments under our agreement with Sobi;
- our ability to identify additional collaborators 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 of pegcetacoplan in other jurisdictions and indications and other product candidates we may pursue;
- 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 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 pegcetacoplan in other jurisdictions and indications and our other 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;

- the effect of the COVID-19 pandemic on the healthcare system and the economy generally and on our clinical trials and other operations specifically;
- our ability to obtain adequate reimbursement for EMPAVELI in the United States or any other product we commercialize; and
- the costs of operating as a public company.

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, 2021:

(In thousands)	Payments Due by Period				
	Total	Less than 1 Year	1-3 Years	3-5 Years	More than 5 Years
SFJ agreement	$ 456,000	$ 34,500	$ 154,250	$ 212,000	$ 55,250
Convertible notes (1)	223,620	6,719	13,439	203,462	—
Non-cancellable purchase commitments (2)	105,473	53,834	51,639	—	—
Operating leases (3)	25,309	5,560	10,487	8,706	556
Total	$ 810,402	$ 100,613	$ 229,815	$ 424,168	$ 55,806

(1) Amounts include interest on long-term debt obligations under the debt outstanding as of December 31, 2021, applying contractual fixed interest rate and assuming scheduled payments are paid as contractually required through maturity. In January 2021 and July 2021, we entered into agreements to exchange $126.1 million and $201.1 million, respectively, of our Convertible Notes for shares of common stock.

(2) Equals the non-cancellable purchase commitments signed as of December 31, 2021.

(3) 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 in May 2021 and the EMA in December 2021 for the use of systemic pegcetacoplan as a treatment for PNH, we will make annual payments to SFJ following pre-determined, fixed payment schedules as set forth in the SFJ agreement and SFJ amendment. We made a $4.0 million initial payment to SFJ in June 2021 for FDA approval, and the remaining annual payments due to SFJ totaled $456 million as of December 31, 2021, with the first payment of $5.0 million due in January 2022, which we paid in January 2022, with the final payment due in 2027.

We have entered into contracts to conduct research and development activities with third parties which commit us to pay future milestone payments or to pay royalty fees 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. With respect to the license for the ophthalmic field of use, we have agreed to make milestone payments to Penn aggregating up to $3.2 million based on achieving specified development and regulatory milestones, and up to $5.0 million based on achieving specified annual sales milestones. The license agreements also require that we pay low single-digit royalties to Penn based on net sales of each licensed product by us and our affiliates and sublicensees and specified minimum quarterly royalty thresholds. We accrued $0.3 million for royalty obligations to Penn in 2021. In addition, we are obligated to pay Penn a specified portion of income we receive from sublicensees. In January 2021, we paid Penn $25.0 million as a sublicensee fee, in August 2021 we made payments of $1,025,000, net of a credit for the annual license maintenance payment for the achievement of milestones, and as of December 31, 2021 we accrued $5.0 million as a sublicense fee under these agreements relating to the Sobi agreement. 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, 2021, we are obligated to pay up to $2.3 million to these vendors.

We have certain non-cancelable purchase obligations related to the manufacturing of drug substance and drug product, with Bachem, agreeing to purchase a significant portion of our requirements for the pegcetacoplan drug substance over the next five years and a commercial supply agreement with NOF Corporation, or NOF, to purchase activated polyethylene glycol derivative, or PEG, which is a component of pegcetacoplan. Under these agreements, as of December 31, 2021, we are obligated to pay up to an aggregate of $102.5 million to these vendors. In addition, we have other non-cancelable purchase agreements as of December 31, 2021, where we are obligated to pay up to an aggregate of $3.0 million to these vendors.

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, 2021, we had cash, cash equivalents and marketable securities of $700.6 million, consisting primarily of money market funds and U.S. treasury securities. 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 Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Apellis Pharmaceuticals, Inc. and subsidiaries (the "Company") as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows, for each of the three years in the period ended December 31, 2021, 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, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, 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, 2021, 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 28, 2022, expressed an unqualified opinion on the Company's internal control over financial reporting.

Change in Accounting Principle

As discussed in Note 1 to the financial statements, the Company has changed its method of accounting for convertible debt in fiscal year 2021 due to the adoption of ASU 2020-06, *Debt – Debt with Conversion and Other Options (Subtopic 470-20)*.

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.

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 Liability — Refer to Notes 6 and 12 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 the Company's clinical trials ("SFJ Agreement"). The SFJ Agreement was presented as a derivative liability whose fair value was based on unobservable inputs. The liability was 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. Subsequent to regulatory approval on December 15, 2021, the development derivative liability was remeasured and then reclassed from a derivative to a development liability which will be accreted from the initial carrying value to the total payment amount using the effective interest rate method.

We identified the valuation of the development liability at December 15, 2021 as a critical audit matter. The development liability

was valued using a discounted cash flow method whereby the cash flows are present valued using a risk-adjusted discount rate. This model includes inputs that are indexed to comparable market data. 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 liability model and the cost of borrowing 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 the review of the discount rate.

- With the assistance of our fair value specialists, we evaluated the reasonableness of the valuation methodology including the discount rate used by testing the source information and the mathematical accuracy of the calculation.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
February 28, 2022

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

APELLIS PHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS
(Amounts in thousands, except per share amounts)

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 640,192	$ 565,779
Marketable securities	60,358	311,869
Accounts receivable	10,103	—
Inventory	16,286	—
Prepaid assets	24,868	11,400
Restricted cash	1,563	1,266
Other current assets	70,677	26,878
Total current assets	824,047	917,192
Non-current assets:		
Right-of-use assets	19,901	17,719
Property and equipment, net	6,177	6,803
Other assets	31,640	18,855
Total assets	$ 881,765	$ 960,569
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 16,909	$ 8,477
Accrued expenses	103,239	111,935
Current portion of development liability	7,584	—
Current portion of development derivative liability	—	4,230
Current portion of right-of-use liabilities	4,115	3,685
Total current liabilities	131,847	128,327
Long-term liabilities:		
Long-term development liability	345,151	—
Convertible senior notes	189,024	358,830
Development derivative liability	—	253,638
Right-of-use liabilities	17,081	15,217
Total liabilities	683,103	756,012
Commitments and contingencies (Note 16)	—	—
Stockholders' equity:		
Preferred stock, $0.0001 par value; 10,000 shares authorized and zero shares issued and outstanding at December 31, 2021 and 2020	—	—
Common stock, $0.0001 par value; 200,000 shares authorized at December 31, 2021 and 2020; 97,524 and 76,130 shares issued and outstanding at December 31, 2021 and 2020, respectively	10	8
Additional paid-in capital	1,857,430	1,131,013
Accumulated other comprehensive loss	(2,090)	(117)
Accumulated deficit	(1,656,688)	(926,347)
Total stockholders' equity	198,662	204,557
Total liabilities and stockholders' equity	$ 881,765	$ 960,569

See accompanying notes to consolidated financial statements

APELLIS PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(Amounts in thousands, except per share amounts)

	Year Ended December 31,		
	2021	2020	2019
Revenue:			
Product Revenue, net	$ 15,147	$ —	$ —
Licensing and other revenue	51,416	250,646	—
Total revenue:	66,563	250,646	—
Operating expenses:			
Cost of sales	200	—	—
Research and development	345,869	299,921	220,969
Cost of research collaboration	75,000		
License expense	5,000	25,050	—
General and administrative	176,771	139,401	67,046
Operating expenses:	602,840	464,372	288,015
Net operating loss	(536,277)	(213,726)	(288,015)
Loss on extinguishment of debt	—	—	(1,501)
Loss on conversion of debt	(100,589)	—	—
Loss from remeasurement of development derivative liability	(97,675)	(103,029)	(14,839)
Interest income	418	4,164	5,108
Interest expense	(13,241)	(29,937)	(5,285)
Other income/(expense), net	1,362	(501)	(175)
Net loss before taxes	(746,002)	(343,029)	(304,707)
Income tax expense	352	1,845	-
Net loss	$ (746,354)	$ (344,874)	$ (304,707)
Other comprehensive income/(loss):			
Unrealized gain/(loss) on marketable securities	9	(8)	—
Foreign currency gain/(loss)	(1,982)	45	(31)
Total other comprehensive (loss)/income	(1,973)	37	(31)
Comprehensive loss, net of tax	$ (748,327)	$ (344,837)	$ (304,738)
Net loss per common share, basic and diluted	$ (8.84)	$ (4.59)	$ (4.90)
Weighted-average number of common shares used in net loss per common share, basic and diluted	84,421	75,163	62,229

See accompanying notes to consolidated financial statements

APELLIS PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY
(Amounts in thousands, except per share amounts)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Outstanding Shares	Amount				
Balance at January 1, 2019	56,279	$ 6	$ 437,856	$ (123)	$ (276,766)	$ 160,973
Issuance of common stock in follow-on offering, net of offering costs	6,900	—	109,581	—	—	109,581
Issuance of common stock upon exercise of stock options or warrants	759	—	3,129	—	—	3,129
Recognition of equity component of convertible notes	—	—	72,520	—	—	72,520
Purchase of capped call transactions and associated costs	—	—	(28,380)	—	—	(28,380)
Share-based compensation expense	—	—	21,144	—	—	21,144
Net loss	—	—	—	—	(304,707)	(304,707)
Foreign currency gain/(loss)	—	—	—	(31)	—	(31)
Balance at December 31, 2019	63,938	6	615,850	(154)	(581,473)	34,229
Issuance of common stock in follow-on offering, net of offering costs	10,925	1	381,422	—	—	381,423
Issuance of common stock upon exercise of stock options or warrants	1,208	1	9,417	—	—	9,418
Recognition of equity component of convertible notes	—	—	120,485	—	—	120,485
Purchase of capped call transactions and associated costs	—	—	(43,112)	—	—	(43,112)
Share-based compensation expense	—	—	45,376	—	—	45,376
Issuance of common stock to employee stock purchase plan	59	—	1,575	—	—	1,575
Unrealized loss on available-for-sale investments	—	—	—	(8)	—	(8)
Net loss	—	—	—	—	(344,874)	(344,874)
Foreign currency gain/(loss)	—	—	—	45	—	45
Balance at December 31, 2020	76,130	8	1,131,013	(117)	(926,347)	204,557
Adoption of ASU 2020-06	—	—	(165,747)	—	16,013	(149,734)
Issuance of common stock in follow-on offering, net of offering costs	10,063	1	380,361	—	—	380,362
Issuance of common stock upon exercise of stock options	1,063	—	14,691	—	—	14,691
Issuance of shares in exchange of 2019 and 2020 Convertible Notes, including issuance cost	10,065	1	421,092	—	—	421,093
Forfeiture of accrued interest in exchange of 2019 and 2020 Convertible Notes	—	—	4,171	—	—	4,171
Vesting of restricted stock units, net of shares withheld for taxes	91	—	(1,788)	—	—	(1,788)
Share-based compensation expense	—	—	70,667	—	—	70,667
Issuance of common stock to employee stock purchase plan	112	—	2,970	—	—	2,970
Unrealized gain on available-for-sale investments	—	—	—	9	—	9
Net loss	—	—	—	—	(746,354)	(746,354)
Foreign currency gain/(loss)	—	—	—	(1,982)	—	(1,982)
Balance at December 31, 2021	97,524	$ 10	$ 1,857,430	$ (2,090)	$ (1,656,688)	$ 198,662

See accompanying notes to consolidated financial statements

APELLIS PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(Amounts in thousands, except per share amounts)

	Year Ended December 31,		
	2021	2020	2019
Operating Activities			
Net loss	$ (746,354)	$ (344,874)	$ (304,707)
Adjustments to reconcile net loss to net cash used in operating activities:			
Share-based compensation expense	70,667	45,376	21,144
Loss on conversion of debt	100,589	—	
Loss on early extinguishment of debt	—	—	1,501
Loss from remeasurement of development derivative liability	97,675	103,029	14,839
Forfeiture of accrued interest in exchange of convertible notes	4,171	—	—
Depreciation expense	1,379	637	240
Amortization of debt discounts	—	—	52
Amortization of right of use assets	113	222	356
Amortization of term loan facility discounts	—	—	104
Amortization of discounts for convertible notes, net of financing costs	964	15,536	2,186
Accretion of discount to development liability	1,192	—	—
Changes in operating assets and liabilities:			
Accounts receivable	(10,103)	—	—
Inventory	(16,317)	—	—
Prepaid assets	(13,487)	8,738	4,531
Other current assets	(40,928)	(26,284)	287
Other assets	(12,782)	(17,860)	(323)
Accounts payable	10,487	(54)	(1,641)
Accrued expenses	(10,392)	55,046	50,454
Other liabilities	—	—	(158)
Net cash used in operating activities	(563,126)	(160,488)	(211,135)
Investing Activities			
Purchase of property and equipment	(1,103)	(5,422)	(1,693)
Purchase of available-for-sale securities	(171,281)	(879,067)	—
Proceeds from maturity of available-for-sale securities	420,000	567,500	—
Net cash used in investing activities	247,616	(316,989)	(1,693)
Financing Activities			
Proceeds from issuance of common stock, net of issuance costs	380,363	381,423	109,581
(Payments for)/Proceeds from development derivative liability	(4,000)	20,000	120,000
Payments for capped call transactions and associated costs	—	(43,112)	(28,380)
Proceeds from issuance of convertible notes, net of issuance costs	—	322,874	212,912
Proceeds from exercise of stock options and warrants	14,691	9,418	3,129
Proceeds from issuance of common stock under employee share purchase plan	2,970	1,575	—
Payments of employee tax withholding related to equity-based compensation	(1,788)	—	—
Repayment of promissory note	—	—	(7,000)
Repayment of term loan facility	—	—	(21,701)
Net cash provided by financing activities	392,236	692,178	388,541
Effect of exchange rate changes on cash and cash equivalents	(2,016)	359	4
Net increase in cash and cash equivalents	74,710	215,060	175,717
Cash, cash equivalents and restricted cash at beginning of period	567,045	351,985	176,268
Cash, cash equivalents and restricted cash at end of period	$ 641,755	$ 567,045	$ 351,985

See accompanying notes to consolidated financial statements

APELLIS PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(Amounts in thousands, except per share amounts)
(Cont'd)

	Year Ended December 31,		
	2021	2020	2019
Reconciliation of cash, cash equivalents and restricted cash to the consolidated balance sheets:			
Cash and cash equivalents	$ 640,192	$ 565,779	$ 351,985
Restricted cash	1,563	1,266	—
Total cash, cash equivalents, and restricted cash	$ 641,755	$ 567,045	$ 351,985
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 10,265	$ 12,929	$ 987
Equity component of convertible notes	$ —	$ 120,485	$ 72,520
Convertible Notes exchanged for common stock	$ 328,017	$ —	$ —

See accompanying notes to consolidated financial statements

1. Nature of Organization and Operations

Apellis Pharmaceuticals, Inc. (the "Company") is a commercial-stage biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutic compounds to treat diseases with high unmet needs 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.

The Company's operations since inception have been limited to organizing and staffing the Company, acquiring rights to product candidates, business planning, raising capital, developing its product candidates, and commercializing EMPAVELI (pegcetacoplan) for the treatment of paroxysmal nocturnal hemogobinuria, or PNH.

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"). Additionally, the Company is subject to risks arising from the Coronavirus Disease 2019 (COVID-19) pandemic, which could have adverse effects upon its business and operations, including on its ability to initiate, conduct and complete clinical trials, and could disrupt regulatory activities.

Adoption of ASU 2020-06 Debt – Debt with Conversion and Other Options (Subtopic 470-20)

Effective January 1, 2021, the Company early adopted ASU 2020-06, Debt – Debt with Conversion and Other Options (Subtopic 470-20) which reduces complexity in applying GAAP to certain financial instruments with characteristics of liability and equity. The ASU removes the guidance that requires entities to account for beneficial conversion features and cash conversion features in equity, separately from the host convertible debt or preferred stock. The ASU further revises the guidance to require entities to calculate diluted earnings per share for convertible instruments by using the if-converted method. In addition, entities must presume share settlement for purposes of calculating diluted earnings per share when an instrument may be settled in cash or shares. The impact of the adoption of the statement increased net debt outstanding and decreased net equity by $149.7 million as of January 1, 2021. Of the $149.7 million decrease to net equity, $16.0 million was recorded to retained earnings. See Note 8, Long Term Debt for additional information.

Collaboration and License Agreement

On October 27, 2020, the Company and its wholly-owned subsidiaries Apellis Switzerland GmbH and APL DEL Holdings, LLC entered into a Collaboration and License Agreement with Sobi, concerning the development and commercialization of pegcetacoplan and specified other structurally and functionally similar compstatin analogues or derivatives for use systemically or for local non-ophthalmological administration (collectively referred to as the "Licensed Products").

Under the collaboration agreement, the Company granted Sobi an exclusive (subject to certain retained rights of the Company), sublicensable license of certain patent rights and know-how to develop and commercialize Licensed Products in all countries outside of the United States. The Company retained the right to commercialize Licensed Products in the United States, and, subject to specified limitations, to develop Licensed Products worldwide for commercialization in the United States.

Sobi paid the Company an upfront payment of $250.0 million in November 2020 and has agreed to pay up to an aggregate of $915.0 million upon the achievement of specified one-time regulatory and commercial milestone events, and to reimburse the Company for up to $80.0 million in development costs. The Company will also be entitled to receive tiered, double-digit royalties (ranging from high teens to high twenties) on sales of Licensed Products outside of the United States, subject to customary deductions and third-party payment obligations, until the latest to occur of: (i) expiration of the last-to-expire of specified licensed patent rights; (ii) expiration of regulatory exclusivity; and (iii) ten (10) years after the first commercial sale of the applicable Licensed Product, in each case on a Licensed Product-by-Licensed Product and country-by-country basis. Under the collaboration agreement, the Company remains responsible for its license fee obligations (including royalty obligations) to the University of Pennsylvania as a licensor of the Company and for its payment obligations to SFJ Pharmaceuticals. See note 13, License and Collaboration Agreements, for further discussion related to the Sobi collaboration agreement.

Convertible Notes Exchange

On January 6, 2021, the Company entered into separate, privately negotiated exchange agreements with certain holders of its convertible notes issued in September 2019 (the "2019 Convertible Notes"). Under the terms of these exchange agreements, the holders exchanged approximately $126.1 million in aggregate principal amount of 2019 Convertible Notes held by them for an aggregate of 3,906,869 shares of common stock. The Company also issued 69,491 shares for settlement of issuance costs paid to the Company's advisor. The Company recognized a total loss on conversion of debt in consolidated statement of operations of $39.5 million.

In July 2021, the Company entered into separate, privately negotiated exchange agreements to modify the conversion terms with certain holders of the 2019 Convertible Notes and the 2020 Convertible Notes issued in May 2020 (the "2020 Convertible Notes", and together with the 2019 Convertible Notes, the "Convertible Notes"). Under the terms of these exchange agreements, the holders exchanged approximately $201.1 million in aggregate principal amount of Convertible Notes held by them for an aggregate of 5,992,217 shares of common stock issued by the Company. The Company also has agreed to issue 78,419 shares for settlement of issuance costs paid to the Company's advisor. The Company recognized a total loss on conversion of $61.1 million during the year ended December 31, 2021.

The conditional conversion feature of the Convertible Notes was triggered as of June 30, 2021, and so the Convertible Notes were convertible at the option of the holders, in whole or in part, between July 1, 2021 and September 30, 2021. From July 1, 2021, we had received conversion requests for the Convertible Notes for the conversion of approximately $0.7 million in aggregate principal amount of Convertible Notes. We issued an aggregate of 18,775 shares of common stock to settle these conversions requests in October 2021.

As of December 31, 2021, the Company held in treasury Convertible Notes in the principal amount of $327.2 million which notes have not been cancelled. See Note 8, Long Term Debt for additional information.

Capped Call Transactions

On May 6, 2020, concurrently with the pricing of the 2020 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 the 2020 Convertible Notes and/or offset any cash payments the Company is required to make in excess of the principal amount of converted 2020 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 2020 Convertible Notes) and is subject to anti-dilution adjustments substantially similar to those applicable to the conversion rate of such 2020 Convertible Notes.

Follow-on Public Offerings

On November 18, 2021, the Company issued and sold 10,062,500 shares of its common stock at a price per share to the public of $40.00 in a follow-on public offering including an additional 1,312,500 shares of its common stock that were sold at the follow-on public offering price of $40.00 per share pursuant to the underwriters' agreement in full exercise of their option to purchase additional shares of common stock. The Company received net proceeds of approximately $380.4 million after deducting underwriting discounts and commissions of approximately $22.1 million and offering costs of $0.6 million for these transactions.

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' agreement in full exercise of their option to purchase additional shares of common stock. The Company received net proceeds of approximately $381.4 million after deducting underwriting discounts and commissions of approximately $22.2 million and offering costs of $0.5 million for these transactions.

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. As of February 28, 2022, the date of issuance of these consolidated financial statements, the Company believes that its cash and cash equivalents and marketable securities as of December 31, 2021 of $700.6 million, 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 Bermuda Limited, Apellis Germany GmbH, Apellis Ireland Ltd, Apellis Netherlands B.V., Apellis Switzerland GmbH, Apellis UK Limited, APL DEL Holdings LLC, APL Sales Corp I, LLC, APL PRG I, Corp., Apellis Cayman Holdings, Ltd., APL DEL Holdings II, LLC and Apellis MA Securities Corp. 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").

Revenue Recognition

The Company's revenues consist of product sales of EMPAVELI and revenue derived from its collaboration arrangement with Sobi. See Note 13, License and Collaboration Agreements for further discussion related to the Sobi Collaboration and License Agreement.

The Company accounts for contracts with its customers in accordance with FASB ASC Topic 606, *Revenue from Contracts with Customers, (*"ASC 606"). Pursuant to ASC 606, for arrangements or transactions between participants determined to be within the scope of the contracts with customers guidance, the Company performs the following five steps to determine the appropriate amount of revenue to be recognized as the Company fulfills its obligations: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation.

Revenue is recognized when, or as, the Company satisfies a performance obligation by transferring a promised good or service to a customer. An asset is transferred when, or as, the customer obtains control of that asset. For performance obligations that are satisfied over time, the Company recognizes revenue using an input or output measure of progress that best depicts the satisfaction of the relevant performance obligation.

Product Revenue

In 2021, the Company's revenue from net product sales was generated in the United States following the FDA's approval for marketing of EMPAVELI for the treatment of PNH in May 2021. The Company sells EMPAVELI principally through arrangements with specialty pharmacies ("SPs") and specialty distributors ("SDs"), who are the Company's customers. The customers subsequently resell the product to patients and health care providers. The Company applies the ASC 606 five step process discussed above to the contracts with SPs and SDs. The Company provides limited right of return to the customers in cases of shipment errors or expiring or defective products. Product revenues are recognized when the customers take control of the product, which typically occurs upon delivery to the customers.

The Company recognizes revenue from product sales at the net sales price which includes estimates of variable consideration for which reserves are established and reflects each of these as a reduction to the revenue. Overall, these reserves reflect the Company's best estimates of the amount of consideration to which the Company is entitled based on the terms of the contract. The amount of

variable consideration that is included in the transaction price may be constrained. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results in the future vary from estimates, the Company may need to adjust its estimates, which would affect net revenue in the period of adjustment. The following are the Company's significant categories of variable consideration:

Distribution Fees: Distribution fees include distribution service fees paid to SPs and SDs based on a contractually fixed percentage of the wholesale acquisition cost (WAC), fees for data, and prompt payment discounts. The Company does not receive a distinct good or service in exchange for the payment. Distribution fees are recorded as an offset to revenue based on contractual terms at the time revenue from the sale is recognized.

Chargebacks: Chargebacks are discounts and fees related to contracts with various third-party payers including pharmacy benefit managers, private healthcare insurers and government healthcare programs that purchase from SDs at a discounted price. SDs charge back to the Company the difference between the price initially paid by SDs and the discounted price paid to SDs by these entities. The Company issues credit notes for the chargeback which are applied to future sales.

Product Returns: Consistent with industry practice, the Company offers SPs and SDs limited product return rights for shipment errors or expiring or defective products; provided that the return is within a specified period around the product expiration date as set forth in the applicable individual distribution agreement. The Company does not allow product returns for product that has been dispensed to a patient. As the Company receives inventory reports from SPs and SDs and has visibility into the inventory distribution channel, it is able to make a reasonable estimate of future potential product returns based on this on-hand channel inventory data and sell-through data obtained from SPs and SDs. In arriving at its estimate for product returns, the Company also considers historical product returns (to the extent available), the underlying product demand, and industry data specific to the specialty pharmaceutical distribution industry.

Licensing and Collaboration Revenue

The Company analyzes license and collaboration arrangements pursuant to FASB ASC Topic 808, *Collaborative Arrangement Guidance and Considerations*, ("ASC 808") to assess whether such arrangements, or transactions between arrangement participants, involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities or are more akin to a vendor-customer relationship. In making this evaluation, the Company considers whether the activities of the collaboration are considered to be distinct and deemed to be within the scope of the collaborative arrangement guidance or if they are more reflective of a vendor-customer relationship and, therefore, within the scope of ASC 606. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement.

For elements of collaboration arrangements that are not accounted for pursuant to guidance in ASC 606, an appropriate recognition method is determined and applied consistently, generally by analogy to the revenue from contracts with customers guidance. Amounts related to transactions with a counterparty in a collaborative arrangement that is not a customer are presented as collaboration revenue and in a separate line item from revenue recognized from contracts with customers, if any, in our consolidated statements of operations.

Pursuant to ASC 606, for arrangements or transactions between arrangement participants determined to be within the scope of the contracts with customers guidance, the Company performs the five-step process discussed above to determine the appropriate amount of revenue to be recognized as the Company fulfills its obligations.

We evaluate the performance obligations promised in the contract that are based on goods and services that will be transferred to the customer and determine whether those obligations are both (i) capable of being distinct and (ii) distinct in the context of the contract. Goods or services that meet these criteria are considered distinct performance obligations. The Company estimates the transaction price based on the amount expected to be received for transferring the promised goods or services in the contract. The consideration may include fixed consideration or variable consideration. At the inception of each arrangement that includes variable consideration, the Company evaluates the amount of potential transaction price and the likelihood that the transaction price will be received. The Company utilizes either the most likely amount method or expected value method to estimate the amount expected to be received based on which method best predicts the amount expected to be received. The amount of variable consideration that is included in the transaction price may be constrained and is included in the transaction price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. We assess if these options provide a material right to the customer and, if so, these options are considered performance obligations. The Company has not currently identified any such material rights.

Revenue is recognized when, or as, the Company satisfies a performance obligation by transferring a promised good or service to a customer. An asset is transferred when, or as, the customer obtains control of that asset. For performance obligations that are satisfied over time, the Company recognizes revenue using an input or output measure of progress that best depicts the satisfaction of the relevant performance obligation.

After contract inception, the transaction price is reassessed at every period end and updated for changes such as resolution of uncertain events. Any change in the overall transaction price is allocated to the performance obligations on the same methodology as at contract inception.

See Note 13, License and Collaboration Agreements, for further discussion related to the Sobi collaboration agreement.

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 statement on Form S-3 in 2019, and to the Company's offering of Convertible Notes in 2020 and 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.

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

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 8, Long-term Debt, Note 10, Marketable Securities, and Note 12, Fair Value Measurements, include cash and cash equivalents, accounts payable and accrued liabilities. Management believes that the carrying amounts of cash and cash equivalents, 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. See Note 12, Fair Value Measurements, for additional information.

Accounts Receivable

The Company's accounts receivable primarily arise from product sales. They are generally stated at the invoiced amount and do not bear interest. The Company recognizes revenue from product sales at the net sales price which includes estimates of variable consideration for which reserves are established and reflects each of these as a reduction to the revenue. Overall, these reserves reflect the Company's best estimates of the amount of consideration to which the Company is entitled based on the terms of the contract. The amount of variable consideration that is included in the transaction price may be constrained. The accounts receivable from product sales represents receivables due from the Company's SPs or SDs. The Company has had no historical write offs of its accounts receivable, and its payment terms are generally 30-65 days. The Company monitors the financial performance and creditworthiness of its customers and provides reserves against trade receivables for expected credit losses that may result from a customer's inability to pay. Amounts determined to be uncollectible are written-off against the established reserve. As of December 31, 2021, the credit profiles for the Company's customers were deemed to be in good standing and an allowance for credit losses was not considered necessary.

Inventory

Inventory is recorded at the lower of cost or net realizable value, with cost determined on a first-in, first-out basis. Inventory costs include third-party contract manufacturing, third-party packaging services, and freight. The Company primarily uses actual costs to determine the cost basis for its inventory. The Company periodically reviews its inventories to identify obsolete, slow moving, excess or otherwise unsaleable items. The determination of whether inventory costs will be realizable requires estimates by management. The Company does not have any obsolete inventory as of December 31, 2021.

Prior to regulatory approval of its product candidates, the Company expensed costs associated with the manufacturing of its product candidates to research and development expense unless the Company was reasonably certain such costs have future commercial use and net realizable value. When the Company believes regulatory approval and subsequent commercialization of our product candidates is probable, and the Company also expects future economic benefit from the sales of the product candidates to be realized, the Company will then capitalize the costs of production as inventory.

Prior to receiving FDA approval for EMPAVELI on May 14, 2021, the Company included in research and development expense the costs associated with the manufacture of EMPAVELI inventory to be sold upon commercialization. As a result, the manufacturing costs related to the EMPAVELI inventory build-up incurred before FDA approval were expensed, totaling approximately $60.4 million in a prior period and are, therefore, excluded from the cost of goods sold for the year ended December 31, 2021.

Development Derivative Liability and Development Liability

Prior to obtaining Regulatory Approval, the development derivative liability was recorded at fair value 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 liability was remeasured quarterly with any change in fair value recorded in loss from remeasurement of development derivative liability on the consolidated statements of operations and comprehensive loss.

Following the EMA approval obtained on December 15, 2021, the Company will make annual payments to SFJ following pre-determined, fixed payment schedules as set forth in the SFJ agreement and SFJ amendment. The Company made a $4.0 million initial payment to SFJ in June 2021 for FDA approval, and, as of December 31,2021, the remaining annual payments due to SFJ totaled $456.0 million, with the first payment of $5.0 million due in January 2022 and the final payment due in 2027. As the variability of the future payments derived from the underlying contingency (i.e., EMA approval and FDA approval) no longer exist, the Company remeasured the development derivative liability on December 15, 2021 and reclassified it from development derivative liability to development liability, with subsequent accounting to follow an effective interest accretion schedule to the fixed payment amounts.

From December 15, 2021 and thereafter until the final annual payment due December 2027, the development liability will be accreted from its initial carrying amount to the total payment amount using the effective interest rate method under ASC 835 over the remaining life of the SFJ agreement. The difference between the carrying amount and the total payment amount is presented as discount to the development liability. The accretion is recorded as interest expense in the consolidated income statement.

Foreign Currency

The financial position and results of operations of the Company's Australian, Irish and German 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 respective periods. 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. The financial position and results of operations of the Company's Swiss subsidiary are measured and reported in U.S. dollars and transactions are translated to U.S. dollars at the end of the period.

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.

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, 2021 and 2020, the Company did not have any significant uncertain tax positions.

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, Netherlands, Switzerland, Australia, Ireland and Germany. 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 foreign currency gains/losses recorded from the remeasurement of the long-term intra-entity loan transaction to the Company's wholly owned subsidiaries, foreign currency gain/loss from the translation of the Company's wholly owned subsidiaries into U.S. dollars, and unrealized gains and losses on marketable securities.

Recent Accounting Pronouncements

In August 2020, the FASB issued ASU 2020-06, *Debt – Debt with Conversion and Other Options (Subtopic 470-20)* to reduce complexity in applying GAAP to certain financial instruments with characteristics of liability and equity. The ASU removes the guidance that requires entities to account for beneficial conversion features and cash conversion features in equity, separately from the host convertible debt or preferred stock. The ASU further revises the guidance to require entities to calculate diluted earnings per share for convertible instruments by using the if-converted method. In addition, entities must presume share settlement for purposes of calculating diluted EPS when an instrument may be settled in cash or shares. The new standard is effective for annual reporting periods beginning after December 15, 2021, for public companies, including interim periods within that reporting period. Early adoption is permitted, but no earlier than fiscal years beginning after December 15, 2020. The Company early adopted this statement effective January 1, 2021. The impact of the adoption of the statement is to increase debt and decrease equity by the amount of the equity component of convertible notes recognized in equity. Additionally, interest expense is expected to decrease by the non-cash portion of the discount amortization. Weighted average basic earnings per share amounts are not expected to be materially affected.

3. Product Revenues, Accounts Receivable, and Reserves for Product Sales

The Company received FDA approval for the sale of EMPAVELI in the United States in May 2021. The Company's product revenues, net of sales discounts and allowances and reserves, as of December 31, 2021 consist of $15.1 million of sales of EMPAVELI to SPs and SDs. The Company did not have product revenue in 2020.

The Company's accounts receivable balance of $10.1 million as of December 31, 2021 consists of EMPAVELI product sales receivable, net of discounts and allowances of $0.2 million. The Company does not have a reserve against its receivable balance.

The Company's product sales reserves totaling $1.0 million are included in accrued expenses on the Company's consolidated balance sheet as of December 31, 2021. The Company did not have accounts receivable or product reserve balances as of December 31, 2020.

4. Inventory

The Company's inventory of EMPAVELI as of December 31, 2021 consisted of $0.5 million of finished goods, $10.1 million of semi-finished goods and $5.7 million of raw material. The Company did not have inventory as of December 31, 2020.

5. Common Stock

The Company has reserved the following shares of common stock for future issuance (in thousands):

	December 31,		
	2021	2020	2019
Shares reserved under 2017 Equity Incentive Plan	11,014	8,613	6,319
Shares reserved under 2017 Employee Stock Purchase Plan	801	913	972
Total	11,815	9,526	7,291

6. Development Derivative Liability and Development 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 $60.0 million following the signing of the agreement and agreed to pay the Company up to an additional $60.0 million 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.

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 $20.0 million funding payment to the Company to support the development of systemic pegcetacoplan for the treatment of patients with PNH.

As of January 29, 2020, the Company had received a total of $140.0 million from SFJ as the Company met milestones as identified in the agreement. The Company did not receive any additional funds from SFJ after January 29, 2020 and in the years ended December 31, 2021 and December 31, 2020.

Under the SFJ agreement, following regulatory approval by the FDA for the use of systemic pegcetacoplan as a treatment for PNH, the Company will be obligated to pay SFJ an initial payment of $4.0 million and then an additional $226.0 million in the aggregate in six additional annual payments with the majority of the payments being made from the third anniversary to the sixth anniversary of regulatory approval. The Company obtained the FDA approval on May 14, 2021 and paid to SFJ the initial payment of $4.0 million on June 17, 2021. The subsequent annual payments are due and payable in May each year from 2022 to 2027.

Under the SFJ agreement if regulatory approval is granted by the EMA for the use of systemic pegcetacoplan as a treatment for PNH, the Company will be obligated to pay SFJ an initial payment of $5.0 million and then an additional $225.0 million in the aggregate in six additional annual payments with the majority of the payments being made from the third anniversary to the sixth anniversary of regulatory approval. The Company obtained the EMA approval on December 15, 2021. The initial payment of $5.0 million was paid in January 2022, and subsequent annual payments are due and payable in December each year from 2022 through 2027.

Additionally, the Company granted a security interest to SFJ 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.

Prior to the EMA approval on December 15, 2021, the SFJ Agreement is presented as a derivative liability on the consolidated balance sheet and, as such, is recorded at fair value and remeasured each quarter. The total changes in fair value of $97.7 million and $103.0 million were recorded for the years ended December 31, 2021 and 2020, respectively, in loss from remeasurement of development derivative liability in the consolidated income statement. The remeasurement of the development derivative liability resulted in a remeasured fair value of $257.9 million as of December 31, 2020 on the consolidated balance sheet. At December 31, 2020, $4.2 million of the $257.9 million of the development derivative liability fair market value was included in current liabilities.

The following table presents a rollforward of the liability (in thousands):

	For the Year Ended December 31,	
	2021	2020
Balance at fair market value, January 1,	$ 257,868	$ 134,839
Amounts received under the SFJ agreement and SFJ amendment	—	20,000
Amounts repaid under the SFJ Agreement and SFJ Amendment	(4,000)	—
Loss recorded in loss from remeasurement of development derivative liability	97,675	103,029
Reclassification to development liability on December 15	(351,543)	—
Balance at fair market value, December 31	$ —	$ 257,868

The derivative fair value is a Level 3 fair value measurement and 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 EMA approval, (iii) SFJ's cost of borrowing, and (iv) the Company's cost of borrowing.

SFJ's implied cost of borrowing was 8.0% as of December 31, 2020 and December 15, 2021 and the Company's implied cost of borrowing was 12.65% as of December 31, 2020 and 7.91% as of December 15, 2021. 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.

Following the EMA approval obtained on December 15, 2021, the Company will make annual payments to SFJ following pre-determined, fixed payment schedules as set forth in the SFJ agreement and SFJ amendment. The Company made a $4.0 million initial payment to SFJ in June 2021 for FDA approval, and the remaining annual payments due to SFJ total $456.0 million, with the first payment of $5.0 million due in January 2022 and the final payment due in 2027. As the variability of the future payments derived from the underlying contingency (i.e., EMA approval and FDA approval) no longer exist, the Company remeasured the development derivative liability on December 15, 2021 and reclassified it from development derivative liability to development liability, with subsequent accounting to follow an effective interest accretion schedule to the fixed payment amounts.

From December 15, 2021 and thereafter until the final annual payment due December 2027, the development liability will be accreted from its initial carrying amount to the total payment amount using the effective interest rate method under ASC 835 over the remaining life of the SFJ agreement. The difference between the carrying amount and the total payment amount is presented as discount to the development liability. The accretion is recorded as interest expense in the consolidated income statement.

The following table summarizes the development liability (in thousands):

	As of December 31,2021	Effective Interest Rate
Development liability	$ 456,000	7.91%
Less: Unamortized discount to development liability	(103,265)	
Less: Current portion of development liability, net of discount	(7,584)	
Total long term development liability	345,151	

For the period from December 15, 2021 through December 31, 2021, $1.2 million of interest expense was recorded for the accretion of the development liability.

7. Accrued Expenses and Prepaid Assets

Accrued expenses are as follow (in thousands):

	December 31, 2021	December 31, 2020
Accrued research and development	$ 35,217	$ 47,879
Accrued cost of research collaboration	25,000	—
Accrued license fee	5,000	25,050
Accrued payroll liabilities	25,212	22,896
Other	12,810	16,110
Total	$ 103,239	$ 111,935

Prepaid assets include $12.0 million and $8.0 million of prepaid research and development costs as of December 31, 2021 and 2020, respectively.

8. Long-term Debt

Convertible Senior Notes

On September 16, 2019, the Company completed a private offering of the 2019 Convertible Notes with an aggregate principal amount of $220.0 million 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 2019 Convertible Notes were approximately $212.9 million after deducting the initial purchasers' discounts and commissions of $6.6 million and offering expenses of $0.5 million paid by the Company. The Company 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.

On May 12, 2020, the Company issued the 2020 Convertible Notes with an aggregate principal amount of $300.0 million. The net proceeds from the sale of the 2020 Convertible Notes were approximately $322.9 million after deducting the purchasers' discounts and commission of $5.7 million and offering expenses of $0.3 million. The Company used $43.1 million of the net proceeds from the sale to pay the cost of the additional capped call transactions in May 2020 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.

- during any calendar quarter, if the last reported sale price of the Company's common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on, and including, the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day;
- during the five-business day period after any five consecutive trading day period in which the trading price per $1,000 principal amount of the Convertible Notes for each such trading day was less than 98% of the product of the last reported sale price of the Company's common stock and the conversion rate on each such trading day;
- if the Company calls any or all of the Convertible Notes for redemption, at any time prior to the close of business on the second scheduled trading day immediately preceding the redemption date; or
- upon the occurrence of corporate events specified in the Indenture.

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.

The Company used an effective interest rate of 10.5% to determine the liability component of the 2019 and 2020 Convertible Notes. This resulted in the recognition of $145.1 million and $204.5 million as the liability component of the 2019 and 2020 Convertible Notes, respectively, and the recognition of the residual amount of $74.9 million and $95.5 million as the debt discount with a corresponding increase to additional paid in capital for the equity component of the 2019 and 2020 Convertible Notes, respectively. The 2020 aggregate debt issuance costs of $6.0 million were allocated to the liability and equity components in the amounts of $3.7 million and $2.3 million, respectively. The 2019 Convertible Notes aggregate debt issuance costs of $7.1 million were allocated to the liability and equity components in the amounts of $4.7 million and $2.4 million, respectively.

Effective January 1, 2021, the Company adopted ASU 2020-06 using the modified retrospective method. Upon adoption, the Company increased net debt and reduced net equity by $149.7 million. The $149.7 million consisted of several items. The first item is the reclassification from equity to debt of the residual amounts originally identified as the equity components of the 2019 and 2020 Convertible Notes of $74.9 million and $95.5 million, respectively. The equity component reclassification was offset by the adjustment to retained earnings for the reversal of previous non-cash interest expense recorded for the amortization of the equity

components of $17.1 million. The second item is the reclassification from equity to debt of the debt issuance costs originally allocated to equity for the 2019 and 2020 Convertible Notes of $2.4 million and $2.3 million, respectively. The debt issuance costs reclassification was offset by the adjustment to retained earnings for previous amortization of the debt issuance costs recorded of $1.1 million.

In January 2021 and in July 2021, the Company entered into separate, privately negotiated exchange agreements to modify the conversion terms with certain holders of its 2019 Convertible Notes. Under the terms of these exchange agreements, in January 2021 and July 2021, the holders exchanged approximately $126.1 million of 2019 Convertible Notes and $201.1 million of Convertible Notes, respectively, in aggregate principal amount held by them for an aggregate of 3,906,869 shares and 5,992,217 shares, respectively, of common stock issued by the Company. In accordance with ASC topic 470-20, “Debt,– Debt with Conversion and Other Options,” (“ASC 470-20”) the Company accounted for the exchange as an induced conversion based on the short period of time the conversion offer was open and the substantive conversion feature offer. The Company accounted for the conversion of the debt as an inducement by expensing the fair value of the shares that were issued in excess of the original terms of the Convertible Notes.

For the January 2021 transaction, the Company reduced net debt outstanding and increased net equity on the consolidated balance sheet by $122.8 million, consisting of the par value of the 2019 Convertible Notes exchanged of $126.1 million less the $3.3 million of remaining debt issuance costs associated with the exchanged notes. The Company also increased shares outstanding by 3,906,869 shares consisting of 3,196,172 shares issued at the initial conversion rate in the Indenture of 25.3405 plus an additional 710,697 shares. Additionally, the Company issued 69,491 shares as settlement of debt issuance costs paid to the Company’s advisor in connection with the conversion transaction. The Company recorded a loss on conversion of debt of $39.5 million comprised of $36.4 million related to the value of the shares issued in excess of the original conversion terms at the fair market value and $3.1 million for the value of the 69,491 shares issued in payment of issuance costs. Upon exchange of the 2019 Convertible Notes, the holders forfeited accrued interest through the date of the exchange of $1.7 million, which the Company charged to interest expense and to equity.

For the July 2021 transaction, the Company reduced net debt outstanding and increased net equity on the consolidated balance sheet by $197.0 million, consisting of the par value of the 2019 and 2020 Convertible Notes exchanged of $201.1 million less the $4.1 million of remaining debt issuance costs associated with the exchanged notes. The Company also increased shares outstanding by 5,992,217 shares consisting of 5,097,166 shares issued at the initial conversion rate in the Indenture of 25.3405 plus an additional 895,051 shares. Additionally, the Company issued 78,419 shares as settlement of debt issuance costs paid to the Company’s advisor in connection with the conversion transaction. The Company recorded a loss on conversion of debt of $61.1 million comprised of $55.9 million related to the value of the shares issued in excess of the original conversion terms at the fair market value and $5.2 million for the value of the 78,419 shares issued in payment of issuance costs. Upon exchange of the 2019 and 2020 Convertible Notes, the holders forfeited accrued interest through the date of the exchange of $2.5 million, which the Company charged to interest expense and to equity.

The conditional conversion feature of the Convertible Notes was triggered as of June 30, 2021, and so the Notes were convertible at the option of the holders. Certain holders of the Convertible Notes converted approximately $0.7 million of aggregate principal amount of Convertible Notes into an aggregate of 18,775 shares. The shares were issued in October 2021.

The Company recognized a total loss on the conversion of debt of $100.6 million in the Consolidated Statement of Operations and Comprehensive Loss for the year ended December 31, 2021. As of December 31, 2021, the Company held in treasury Convertible Notes in principal amount of $327.2 million which notes had not been cancelled.

Interest expense for the Convertible Notes was $12.0 million and $29.9 million for the years ended December 31, 2021 and 2020, respectively. For the year ended December 31, 2021, interest expense included accrued semi-annual coupon payable of $11.1 million and amortization of debt issuance costs of $0.9 million. For the year ended December 31, 2020, interest expense included amortization of the discount on the Convertible Notes of $15.0 million, accrued semi-annual coupon payable of $14.4 million and amortization of debt issuance costs of $0.5 million. As of December 31, 2021 and 2020, $3.0 million and $7.8 million, respectively 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, 2021 and 2020 was $189.0 million and $358.8 million, respectively.

Capped Call Transactions

On September 11, 2019, and May 6, 2020 concurrently with the pricing of the 2019 Convertible Notes and the 2020 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 $28.4 million and $43.1 million were recorded as reductions to additional paid-in capital at December 31, 2021 for the 2019 and 2020 Convertible Notes, respectively

9. Leases

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.

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, 2021 and 2020, all leases were classified as operating lease assets and liabilities. Additional information related to the operating lease assets and liabilities is as follows (in thousands):

	December 31, 2021	December 31, 2020
Operating lease assets	$ 19,901	$ 17,719
Operating lease liabilities	$ 21,196	$ 18,902
Weighted average remaining term in years	4.66	4.66
Weighted average discount rate used to measure outstanding lease liabilities	7.71%	7.74%

For the years ended December 31, 2021, 2020, and 2019, the total lease cost for operating lease expense was approximately $5.6 million, $4.4 million, and $2.4 million, respectively.

Supplemental cash flow information related to operating leases for the years ended December 31, 2021, 2020 and 2019 is as follows (in thousands):

	2021	2020	2019
Operating cash flows from operating leases	$ 5,989	$ 4,732	$ 2,013
Operating lease assets obtained in exchange for lease obligations	$ 5,675	$ 7,237	$ 10,201

The maturity of the Company's operating lease liabilities as of December 31, 2021 are as follows (in thousands):

2022	$ 5,560
2023	5,625
2024	4,862
2025	4,423
2026 and thereafter	4,839
Total future minimum lease payments	25,309
Less imputed interest	(4,113)
Total operating lease liabilities	$ 21,196

10. Marketable Securities

The amortized cost, gross unrealized holding losses and fair value of available-for-sale debt securities by type of security as of December 31, 2021 were as follows (in thousands):

	As of December 31, 2021			
	Amortized Cost	Gross Unrealized Holding Gains	Gross Unrealized Holding Losses	Fair Value
U.S. Government-related obligations	$ 60,357	$ 3	$ (2)	$ 60,358

	As of December 31, 2020			
	Amortized Cost	Gross Unrealized Holding Gains	Gross Unrealized Holding Losses	Fair Value
U.S. Government-related obligations	$ 311,877	$ 11	$ (19)	$ 311,869

All available-for-sale securities mature in one year or less.

11. Other Comprehensive Income and Accumulated Other Comprehensive Income

The following tables summarize the changes in accumulated other comprehensive income/(loss), by component for the years ended December 31, 2021 and 2020 (in thousands):

	Unrealized Gains (Losses) from Marketable Securities	Foreign Currency Translation Adjustment	Total Accumulated Other Comprehensive Income (Loss)
Balances, December 31, 2020	$ (8)	$ (109)	$ (117)
Net other comprehensive income (loss)	9	(1,982)	(1,973)
Balances, December 31, 2021	$ 1	$ (2,091)	$ (2,090)

	Unrealized Gains (Losses) from Marketable Securities	Foreign Currency Translation Adjustment	Total Accumulated Other Comprehensive Income (Loss)
Balances, December 31, 2019	$ —	$ (154)	$ (154)
Net other comprehensive income (loss)	(8)	45	37
Balances, December 31, 2020	$ (8)	$ (109)	$ (117)

12. 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 (in thousands):

		December 31, 2021			
Balance Sheet Classification:	Type of Instrument	Level 1	Level 2	Level 3	Total
Financial Assets:					
Cash and cash equivalents:	Money market funds	$ 598,833	$ —	$ —	$ 598,833
Total Financial Assets		$ 598,833	$ —	$ —	$ 598,833

		December 31, 2020			
Balance Sheet Classification:	Type of Instrument	Level 1	Level 2	Level 3	Total
Financial Assets:					
Cash and cash equivalents:	Money market funds	$ 427,515	$ —	$ —	$ 427,515
	Bank certificates of deposit	43,577	—	—	43,577
Total Financial Assets		$ 471,092	$ —	$ —	$ 471,092

The Company's Convertible Notes are Level 1 category within the fair value level hierarchy at December 31, 2021 due to the adoption of ASU 2020- 06. The fair value of the Convertible Notes was $290.7 million at December 31, 2021. At December 31, 2020, the Company's Convertible Notes were Level 2 category within the fair value level hierarchy. At December 31, 2020, the fair value of debt was determined using broker quotes in a non-active market for valuation. As of December 31, 2020, the fair value of the debt

component of the Company's Convertible Notes was $676.2 million. 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 sheets at December 31, 2021 and 2020.

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

		December 31, 2021			
Balance Sheet Classification:	Type of Instrument	Level 1	Level 2	Level 3	Total
Financial Assets:					
Marketable securities:	US government obligations	60,358	—	—	60,358
Total Financial Assets		$ 60,358	$ —	$ —	$ 60,358

		December 31, 2020			
Balance Sheet Classification:	Type of Instrument	Level 1	Level 2	Level 3	Total
Financial Assets:					
Cash and cash equivalents:	US government obligations	$ 89,990	$ —	$ —	$ 89,990
Marketable securities:	US government obligations	311,869	—	—	311,869
Total Financial Assets		$ 401,859	$ —	$ —	$ 401,859
Financial Liabilities:					
Development derivative liability	Development derivative liability	$ —	$ —	$ 257,868	$ 257,868
Total Financial Liabilities		$ —	$ —	$ 257,868	$ 257,868

Prior to Regulatory Approval obtained on December 15, 2021, the fair value of the SFJ agreement was presented as a development derivative liability based on Level 3 inputs. The Company remeasured the development derivative liability on December 15, 2021 and reclassified it from development derivative liability to development liability. The derivative was 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 EMA approval, (iii) SFJ's cost of borrowing, and (iv) the Company's cost of borrowing.

SFJ's implied cost of borrowing was 8.0% as of December 15, 2021 and December 31, 2020, and the Company's implied cost of borrowing was 7.91% as of December 15, 2021 and 12.65% as of December 31, 2020. These implied costs of borrowing were determined assuming the SFJ agreement was initially executed with arm's-length terms.

13. License and Collaboration Agreements

Sobi License and Collaboration Agreement

On October 27, 2020, the Company and its subsidiaries Apellis Switzerland GmbH and APL DEL Holdings, LLC entered into a Collaboration and License Agreement with Sobi, concerning the development and commercialization of pegcetacoplan and specified other structurally and functionally similar compstatin analogues or derivatives for use systemically or for local non-ophthalmological administration (collectively referred to as the "Licensed Products").

Under the collaboration agreement, the Company granted Sobi an exclusive (subject to certain retained rights of the Company), sublicensable license of certain patent rights and know-how to develop and commercialize Licensed Products in all countries outside of the United States. The Company retains the right to commercialize Licensed Products in the United States, and, subject to specified limitations, to develop Licensed Products worldwide for commercialization in the United States.

Under the collaboration agreement, the Company and Sobi have agreed to collaborate to develop Licensed Products for the treatment of paroxysmal nocturnal hemoglobinuria, cold agglutinin disease, hematopoietic stem cell transplantation-associated thrombotic microangiopathy, C3 glomerulopathy and immune complex membranoproliferative glomerulonephritis, and amyotrophic lateral sclerosis, and any other indications subsequently agreed upon by the parties, for commercialization by or on behalf of the Company in the United States and by or on behalf of Sobi outside of the United States. If the parties do not agree to jointly pursue any development activities for the Licensed Products (whether for an Initial Indication or otherwise), the party proposing to pursue such

activities may conduct such activities at its sole expense (with the non-proposing party having the right to obtain rights to the data generated by such development activities by paying a specified percentage of that expense), subject to agreed-upon exceptions that limit each party's unilateral development rights.

The initial development plan sets forth the initial development activities to be conducted by each of the Company and Sobi, with the Company bearing all costs incurred in conducting the activities set forth in such initial development plan, as well as certain specified additional costs that are not included in the initial development plan that may be incurred by the parties in developing Licensed Products for paroxysmal nocturnal hemoglobinuria in the European Union and the United Kingdom. The Company and Sobi will form several governance committees to oversee the development and manufacture, and to review and discuss the commercialization, of Licensed Products.

The Company shall supply Licensed Products to Sobi for development and for commercialization outside of the United States in accordance with a supply agreement to be negotiated by the parties. The collaboration agreement grants Sobi the right to perform or have performed drug product manufacturing of Licensed Products for development and for commercialization outside the United States and to manufacture or have manufactured drug substance under certain circumstances.

Sobi paid the Company an upfront payment of $250.0 million in November 2020 and has agreed to pay up to an aggregate of $915.0 million upon the achievement of specified one-time regulatory and commercial milestone events, and to reimburse the Company for up to $80.0 million in development costs. The Company will also be entitled to receive tiered, double-digit royalties (ranging from high teens to high twenties) on sales of Licensed Products outside of the United States, subject to customary deductions and third-party payment obligations, until the latest to occur of: (i) expiration of the last-to-expire of specified licensed patent rights; (ii) expiration of regulatory exclusivity; and (iii) ten (10) years after the first commercial sale of the applicable Licensed Product, in each case on a Licensed Product-by-Licensed Product and country-by-country basis. Under the collaboration agreement, the Company remains responsible for its license fee obligations (including royalty obligations) to the University of Pennsylvania as a licensor of the Company and for its payment obligations to SFJ Pharmaceuticals.

Sobi Accounting Analysis

The Company has determined that the agreement is within the scope of ASC 808 as a contractual arrangement that involves a joint operating activity whereby both parties are (i) active participants in the activity and (ii) exposed to certain significant risks and rewards dependent on the commercial success of the activity. ASC Topic 808 does not address measurement or recognition matters but allows for analogizing to ASC 606. Pursuant to ASC 606, the Company performed the following five steps: (i) identified the contract(s) with a customer; (ii) identified the performance obligations in the contract; (iii) determined the transaction price; (iv) allocated the transaction price to the performance obligations in the contract; and (v) recognized revenue when (or as) the entity satisfies a performance obligation.

The Company identified the following material distinct promises under the Sobi Agreement: (1) licenses to develop and commercialize pegcetacoplan or, Licenses to IP, and (2) performance of research and development services. The Company determined the promises to be distinct because Sobi can benefit from each of the license and the development services on their own or with readily available services. The Company could have provided the license without any development services and Sobi would have been able to benefit from it by obtaining development services from another provider as the Licensed Products are at a more mature stage in their life cycle.

Under the agreement, Sobi agreed to pay the Company

i) a fixed amount of $250.0 million in an upfront payment in November 2020;
ii) a fixed amount of an additional $80.0 million in development reimbursements, payable yearly in four tranches in amounts determined based upon actual expenses incurred by the Company;
iii) up to an aggregate of $915.0 million upon the achievement of specified one-time regulatory and commercial milestone events; and
iv) tiered, double-digit royalties, ranging from high teens to high twenties, on sales of Licensed Products outside of the United States, subject to customary deductions and third-party payment obligations.

At contract inception, the $250.0 million non-refundable payment and the $80.0 million reimbursements were fixed proceeds. The Company evaluated whether Sobi is a customer for either of the distinct promises in the agreement. Under the Licenses to IP, the Company determined that Sobi is a customer as the know-how provided and the right granted by the Company to Sobi are outputs of the Company's business activities for which the Company will receive consideration. With respect to research and development activity, management determined that there is no vendor relationship as performing research and development activities for others is not a part of the Company's ongoing central operations. Based upon the evaluation of the relative fair values, the Company allocated

the purchase price of $250.0 million and the related milestones and royalties to the license of IP and $80.0 million to performance of research and development activities.

The milestone and royalty payments are subject to activities outside the control of the Company. Per ASC 606, the Company considers this to be a customer/ vendor relationship, therefore, the Company will include the regulatory milestone payments in the total transaction price when it is probable that a significant reversal of revenue would not occur in a future period. The Company will recognize commercial milestone and royalty revenue at the later of (i) when the related sales occur or (ii) when the performance obligation to which the commercial milestone or royalty has been allocated has been satisfied. In case of commercial milestone or royalty payments, the Company will recognize revenue in the same period that the sales are completed for which the Company is contractually entitled to the milestone or percentage-based royalty payment. To date, the Company has not recognized any commercial milestone or royalty revenue resulting from any of our licensing arrangements. Management will periodically assess the elements of the contract and re-evaluate revenue recognition as necessary.

Pursuant to ASC 606, the Company has recognized the $250.0 million in revenue as this is the amount allocated to the license. The $80.0 million reimbursement for research and development activities does not constitute a customer/vendor relationship and thus is not in the scope of ASC 606. As ASC 808 does not include recognition guidance, the Company has established an accounting policy to recognize the payments under the reimbursement as a receivable on the balance sheet in an amount that is to be reimbursed based upon expense incurred by the Company, with a contra- research and development expense recognized in the statement of operations, over time as the expenses are incurred.

Under the Sobi collaboration agreement, for the year ended December 31, 2021, we recognized licensing revenue of $50.0 million in licensing revenue related to the probable achievement of the development milestone for first regulatory and reimbursement approval in Europe. For the year ended December 31, 2021, we recognized in the consolidated statement of operations $32.0 million of contra research and development expense relative to the amount expected to be reimbursed under the $80.0 million for research and development incurred expenses. As of December 31, 2021, we have a receivable of $100.0 million, with $70.0 million in current and $30.0 million in long term assets, respectively, on the consolidated balance sheet. If the milestone we consider probable of achievement is not achieved, we will recognize a reversal of $50.0 million in license revenue.

Under the Sobi collaboration agreement, for the year ended December 31, 2020, we recognized $250.0 million of licensing revenue in the consolidated statement of operations. For the year ended December 31, 2020, we also recognized in the consolidated statement of operations $43.0 million of contra research and development expense relative to the amount expected to be reimbursed under the $80.0 million for research and development incurred expenses. We also recognized a corresponding receivable of $43.0 million, with $25.0 million in current and $18.0 million in long term assets, respectively, on the consolidated balance sheet as of December 31, 2020.

University of Pennsylvania License Agreement

The Company is a party to a license agreement with the Trustees of the University of Pennsylvania (“Penn”) for an exclusive, worldwide license to specified patent rights. The Company is required to pay annual maintenance fees of $0.1 million until the first sale of a licensed product. The Company is also required to make milestone payments aggregating up to $3.2 million based upon the achievement of specified development and regulatory milestones and up to $5.0 million 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 $0.1 million until the first sale of a licensed product. The Company is required to make milestone payments aggregating up to $1.7 million, based upon the achievement of development and regulatory approval milestones, and up to $2.5 million, 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 January 2021, the Company paid $25.0 million for sublicense fee owed to Penn related to the Sobi Agreement and another licensing transaction. As of December 31, 2020 the $25.0 million was recognized in accrued expenses on the consolidated balance sheet and recognized in license fees on the consolidated income statement. In August 2021 the Company paid $1.0 million to Penn upon the achievement of a development milestone. Additionally, in December 2021, the Company recorded $5.0 million based on the probable achievement of a development milestone.

Beam Research Collaboration

In June 2021, the Company entered into an exclusive five-year research collaboration with Beam focused on the use of Beam's proprietary base editing technology to discover new treatments for complement-driven diseases. The Company and Beam agreed to collaborate on up to six research programs focused on C3 and other complement targets in the eye, liver and brain. Under the terms of the collaboration agreement, Apellis is responsible for selecting specific genes within the complement system in various organs including the eye, liver and brain (the "Target List") and providing analytical support while Beam will apply its base editing technology and conduct preclinical research on up to six base editing programs for the Target List. During the first five years of the collaboration agreement, Beam is prohibited from developing on its own or with a third party any base editing therapies associated with the items on the Target List but does not prevent Beam from licensing its intellectual property to a third-party for another purpose outside of the Target List. The Company will have exclusive rights to license each of the six programs and will assume responsibility for subsequent development and commercialization. Beam may elect to enter a 50-50 co-development and U.S. co-commercialization agreement with the Company with respect to any one program licensed under the collaboration and upon such election any license agreement in place at that time, would be terminated.

As part of the collaboration, the Company agreed to pay a $50.0 million up-front, non-refundable payment to Beam, which the Company paid in July 2021. The Company is to pay an additional $25.0 million payment on the first anniversary of the agreement on June 30, 2022. The Company and Beam will each be responsible for their own costs during the research collaboration. If and after the opt-in license rights are exercised for each of the up to six programs, Beam will be eligible to receive development, regulatory and sales milestones from the Company, as well as royalty payments on sales. The collaboration has an initial term of five years and may be extended up to two years on a per year program-by-program basis.

The Company analyzed the research collaboration agreement pursuant to ASC 808 to assess whether the agreement involved joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. Since each party is actively participating in this activity and exposed to significant risks and rewards related to the activity through each party's costs will be accounted for under ASC 808.

Since ASC 808 does not provide recognition guidance, the Company referred to the guidance under ASC 730 to arrangements involving payments by the Company. ASC 730 requires the Company to recognize research and developments costs as expense as incurred since the payment was made for the use of Beam's intellectual property and research and development services and there is no alternative use.

The Company recorded the $50.0 million up-front, non-refundable payment to Beam, recorded as a cost of research collaboration in research and development expenses as of December 31, 2021. In addition, for the year ended December 31, 2021, the Company recorded the $25.0 million anniversary payment as a cost of research collaboration in research and development expenses which was considered probable of achievement.

14. 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 2021, 2020 and 2019, the Company recorded $3.1 million, $2.1 million and $0.8 million respectively, for employer contributions made to the 401(k) Plan.

15. Income Taxes

The components of loss from continuing operations before provision for income taxes are as follows (in thousands):

	Year Ended December 31,		
	2021	2020	2019
United States	$ (314,673)	$ (118,839)	$ (297,127)
Foreign	(431,329)	(224,190)	(7,580)
Total	$ (746,002)	$ (343,029)	$ (304,707)

Provision for income taxes for the years ended December 31, 2021, 2020, and 2019 are as follows (in thousands):

	Year Ended December 31, 2021	Year Ended December 31, 2020	Year Ended December 31, 2019
Current income tax expense:			
U.S. Federal	$ —	$ —	$ —
U.S. State and Local	205	57	—
Foreign	147	1,788	—
Total current income tax expense	352	1,845	—
Deferred income tax expense:			
U.S. Federal	—	—	—
U.S. State and Local	—	—	—
Foreign	—	—	—
Total deferred income tax expense	—	—	—
Total tax expense	$ 352	$ 1,845	$ —

A reconciliation between the U.S. federal statutory tax rate and our effective tax rate is summarized as follows (in thousands):

	Year Ended December					
	2021		2020		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	$ (156,660)	21.0%	$ (72,036)	21.0%	$ (63,988)	21.0%
Foreign tax rate differential	38,677	(5.2)	22,760	(6.6)	—	—
State income taxes, net of federal benefit	(14,145)	1.9	(14,107)	4.1	(16,424)	5.4
Change in valuation allowances	133,668	(17.9)	240,065	(69.9)	90,300	(29.6)
Intellectual property transfer	—	—	(162,000)	47.2	—	—
Tax credits	(20,005)	2.6	(11,696)	3.4	(6,113)	2.0
Change in state apportionment	—	—	93	—	(17)	—
Loss on debt conversion	19,548	(2.6)	—	—	—	—
Permanent and other	(731)	0.1	(1,234)	0.3	(3,758)	1.2
Effective income tax provision	$ 352	(0.1)	$ 1,845	(0.5)	$ —	—

The Company's effective income tax rate for the year ended December 31, 2021 compared to the year ended December 31, 2020 decreased primarily as a result of subsidiary operations in foreign jurisdictions.

The Company accounts for income taxes in accordance with ASC Topic 740. Deferred income tax assets and liabilities are determined based upon temporary differences between the financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse.

The following table presents the principal components of the Company's deferred tax assets and liabilities (in thousands):

	December 31,	
	2021	2020
Deferred tax assets:		
Intangible assets	$ 180,963	$ 162,011
Share-based compensation	22,404	11,827
Deferred interest expense	3,925	—
Net operating loss carryforwards	167,160	122,731
Research and development credits	39,672	24,992
Orphan drug credits	23,678	14,372
Development derivative liability	91,183	68,883
Convertible debt	5,551	—
Lease liability	5,029	—
Accruals	5,100	4,520
Other	—	207
Total deferred tax assets	544,665	409,543
Deferred tax liabilities:		
Fixed assets	(69)	(23)
Convertible debt	—	(10,473)
Right-of-use asset	(4,874)	—
481(a) adjustment	(937)	(1,935)
Total deferred tax liabilities	(5,880)	(12,431)
Net deferred tax assets before allowance:	538,785	397,112
Less valuation allowance	(538,785)	(397,112)
Net deferred tax assets	$ —	$ —

ASC Topic 740 requires a valuation allowance to reduce the deferred tax assets reported if, based on the weight of available evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. After consideration of all the evidence, both positive and negative, the Company has recorded full valuation allowances against its domestic and foreign deferred tax assets on December 31, 2021, because management has determined that is it more likely than not that these assets will not be realized. The valuation allowance increased by $141.7 million from December 31, 2020 to December 31, 2021, primarily due to increases in operating losses, development derivative liability, convertible debt transaction and research and development tax credits.

On December 31, 2021, the Company had approximately $355.8 million, $411.2 million and $623.7 million of federal, state and foreign net operating loss carryforward, respectively. On December 31, 2020, the Company had approximately $358.2 million, $405.0 million and $240.9 million of federal, state and foreign net operating loss carryforwards, respectively. The Company also had federal and state research and development tax credit carryforwards $54.2 million and $11.4 million, respectively of as of December 31, 2021. Federal net operating loss carryforward in the amount of $276.9 million may be carried forward indefinitely. The remaining federal and state net operating loss, research and development tax credit carryforwards begin to expire in 2033. The Company's foreign net operating loss carryforwards will begin to expire in 2026.

Under the provisions of the Internal Revenue Code ("IRC"), the net operating loss ("NOL"), and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. NOL 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. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has completed several financings since its inception that it believes may have resulted in a change in control as defined by Sections 382 and 383 of the IRC.

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 on December 31, 2021 or 2020.

The Company and its subsidiaries file income tax returns in the United States, as well as various state and foreign jurisdictions. Generally, the tax years 2018 through 2020 remain open and subject to examination by the major taxing jurisdictions to which the Company is subject. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service, or state or foreign tax authorities, to the extent utilized in a future period.

16. Commitments and Contingencies

The Company contracts to conduct research and development activities with third parties. 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, 2021, the Company would be required to pay certain termination costs and other fees of approximately $2.3 million that would be incurred in future periods.

The Company has certain non-cancelable purchase obligations related to the manufacturing of drug substance and drug product, with Bachem, agreeing to purchase a significant portion of our requirements for the pegcetacoplan drug substance over the next five years and a commercial supply agreement with NOF Corporation, or NOF, to purchase activated polyethylene glycol derivative, or PEG, which is a component of pegcetacoplan. Under these agreements, as of December 31, 2021, we are obligated to pay up to $102.5 million to these vendors. In addition, we have other non-cancelable purchase agreements as of December 31, 2021, where we are obligated to pay up to $3.0 million to these vendors.

Following regulatory approval by the FDA and EMA for the use of pegcetacoplan as a treatment for PNH, the Company has or will have certain payment and other obligations under the SFJ Agreement, which are discussed above in Note 6.

The Company is a party to a master lease agreement under which the Company leases vehicles with initial terms of 36 months from the date of delivery. If the Company were unable to take delivery of a previously ordered vehicle, the Company may incur nominal fees.

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.

17. 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.

As of December 31, 2021, a total of 11,013,982 shares of common stock were reserved for issuance under the 2017 Plan. In January 2022, the shares available for future issuance under the 2017 plan were increased by 3,900,850 shares pursuant to the annual increase described above.

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). In February 2020 the Board of Directors adopted the 2020 Inducement Stock Incentive Plan (the "2020 Plan"), which permitted the Company to grant equity awards to newly hired employees in accordance with Nasdaq listing rule 5635(c)(4). The aggregate number of shares reserved for issuance under the 2020 Plan was initially 750,000 shares but was increased to 1,050,000 shares in January 2021 and to 1,350,000 shares in February 2022.

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 ESPP in October 2019.

Total share-based compensation expense related to the various plans during the years ended was as follows (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Research and development	$ 30,586	$ 21,381	$ 10,683
General and administrative	40,081	23,995	10,461
Total share-based compensation expense	$ 70,667	$ 45,376	$ 21,144

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.

The following table summarizes the Company's stock option activity:

	Shares (in thousands)	Weighted - Average Exercise Price Per Share	Weighted - Average Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding, December 31, 2020	11,736	$ 19.13		
Granted	2,663	48.10		
Exercised	(1,064)	13.82		
Forfeited	(773)	36.53		
Outstanding, December 31, 2021	12,562	$ 24.65		
Options exercisable, December 31, 2021	7,699	$ 16.24	5.84	$ 240,004
Expected to vest, December 31, 2021	4,863	$ 37.95	8.43	$ 51,821

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, 2021.

During the years ended December 31, 2021, 2020 and 2019, the Company granted stock options to purchase an aggregate of 2.7 million, 2.9 million and 4.4 million shares of its common stock, respectively with weighted average grant date fair values of $30.72, $27.52 and $17.31, respectively.

The aggregate intrinsic value of options exercised during the years ended December 31, 2021, 2020 and 2019 were $39.9 million, $38.0 million, and $15.7 million respectively calculated as the difference between the exercise price of the underlying options and the estimated fair value of the common stock for the options on the respective date of exercise.

The fair market value of options vested during the years ended December 2021, 2020 and 2019 was $53.2 million, $33.6 million and $12.9 million, respectively.

On December 31, 2021, unrecognized compensation expense related to unvested options, was $105.1 million, which the Company expects to recognize over an estimated weighted-average period of 2.58 years.

The assumptions used in the Black-Scholes model to estimate the grant date fair value are as follows:

	Year Ended December 31,		
	2021	2020	2019
Risk-free interest rate	0.41 - 1.34%	0.32 - 1.76%	1.42 - 2.56%
Dividend yield	0%	0%	0%
Volatility	71.7 - 74.4%	84.4 - 87.8%	102.6 - 111.2%
Expected terms (years)	5.31 - 6.08	5.31 - 6.08	5.31 - 6.08

Restricted Stock Units— The fair value of RSU's is estimated based upon the closing market price of the Company's common stock on the date of grant. RSUs generally vest annually over a four-year period:

	Number of Stock Units (in thousands)	Weighted Average Grant Date Fair Value Per Share
Unvested Balance at December 31, 2020	502	$ 38.84
Granted	996	45.01
Vested	(129)	39.11
Forfeited	(145)	43.76
Unvested Balance at December 31, 2021	1,224	43.25

The aggregate intrinsic value of restricted grants vested during the year ended December 31, 2021, was $6.3 million. The fair market value of restricted stock units vested during the year ended December 2021 was $5.0 million.

On December 31, 2021, there was approximately $43.1 million of related unrecognized compensation cost which the Company expects to recognize over a remaining weighted average period of 2.89 years.

Employee Stock Purchase Plan—On December 31, 2021, 801,217 shares of common stock remained available for issuance pursuant to the ESPP. Eligible employees who elect to participate in an offering under the ESPP may have up to 15 percent of their earnings withheld, subject to certain limitations, to purchase shares of common stock pursuant to the ESPP. The price of common stock purchased under the ESPP is equal to 85 percent of the lower of the fair market value of the common stock at the commencement date of each offering period or the relevant purchase date. During the year ended December 31, 2021, a total of 112,009 shares of common stock *were* issued under the ESPP at average per share price of $26.52. During the year ended December 31, 2021, the Company recorded cash received from the issuance of stock to the ESPP of $3.0 million and recorded $1.6 million of stock-based compensation expense related to the ESPP.

18. Net Loss per Common Share

The following table presents the calculation of basic and diluted net loss per common share (amounts in thousands except per share amounts):

	Year Ended December 31,		
	2021	2020	2019
Numerator:			
Net loss	$ (746,354)	$ (344,874)	$ (304,707)
Denominator:			
Weighted-average number of common shares used in net loss per common share -- basic and diluted	84,421	75,163	62,229
Net loss per common share -- basic and diluted	$ (8.84)	$ (4.59)	$ (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 (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Convertible notes	4,865	13,177	—
Common stock under option	12,562	11,736	10,854
Restricted stock units	1,224	502	—
Total	18,651	25,415	10,854

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, 2021. 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, 2021, 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, 2021. 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, 2021, 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, 2021 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, 2021 materially affected, or were reasonably likely to materially affect, our internal control over financial reporting.

As a result of the COVID-19 pandemic, beginning in March 2020, certain of our employees began working remotely. We have not identified any material changes in the Company's internal control over financial reporting as a result of these changes to the working environment. We are continually monitoring and assessing the COVID-19 situation to determine any potential impacts on the design and operating effectiveness of our internal controls 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, 2021, 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, 2021, 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, 2021, of the Company and our report dated

February 28, 2022, expressed an unqualified opinion on those financial statements and included an explanatory paragraph regarding the Company's adoption of new accounting standard.

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 28, 2022

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

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 2022 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, 2021, under the headings “Information about our Executive Officers,” “Election of Directors,” “Corporate Governance,” and “ Delinquent Section 16(a) Reports,” 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 Accountant 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 Herewith
		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	10.7	
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	Summary of Non-Employee Director Compensation Program					X
10.11	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	
10.12+	2017 Employee Stock Purchase Plan	S-1/A	333-220941	10/30/2017	10.15	
10.13+	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	
10.14	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	
10.15	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	
10.16	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	
10.17	Fourth Amendment to Lease, dated November 13, 2020, by and between Registrant and NWALP PHOP Property Owner LLC.	10-K	001-38276	2/25/2020	10.17	
10.18	Open Market Sale Agreement℠, dated as of January 20, 2022, by and between Apellis Pharmaceuticals, Inc. and Jefferies LLC.	8-K	001-38276	1/20/2022	1.1	
10.19	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	
10.20	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	
10.21	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	
10.22	Form of Capped Call Transaction Confirmation	8-K	001-38276	5/7/2020	10.1	
10.23+	Amendment No. 1 to 2017 Employee Stock Purchase Plan	10-Q	001-38276	11/2/2020	10.1	
10.25††	Collaboration and License Agreement, dated October 27, 2020, by and among, the Registrant, Apellis Switzerland GmbH, APL DEL holdings, LLC and Swedish Orphan Biovitrum AB (publ)	10-K	001-38276	2/25/2020	10.25	
10.26††	Commercial Supply Agreement, dated December 30, 2020, by and between the Registrant and Bachem Americas, Inc.	10-K	001-38276	2/25/2020	10.25	
10.27††	Amended and Restated Commercial Supply Agreement, dated March 10, 2021, by and between the Registrant, Apellis Switzerland GmbH and NOF Corporation	10-Q	001-38276	4/28/2021	10.1	
10.28	Inducement Stock Incentive Plan	S-8	333-236710	2/27/2020	99.1	
10.29+	Offer Letter, dated as of April 20, 2020, by and between the Registrant and Nur Nicholson					X
10.30+	Offer Letter, dated as of November 16, 2018, by and between the Registrant and Adam Townsend					X
21.1	Subsidiaries of the Registrant					X

23.1	Consent of Deloitte & Touche, 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.
†† Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.
+ 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 28, 2022

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)	February 28, 2022
/s/ Timothy E. Sullivan **Timothy E. Sullivan**	Chief Financial Officer and Treasurer (Principal Financial Officer)	February 28, 2022
/s/ Jim Chopas **Jim Chopas**	Vice President, Corporate Controller and Chief Accounting Officer (Principal Accounting Officer)	February 28, 2022
/s/ Gerald Chan **Gerald Chan**	Director	February 28, 2022
/s/ A. Sinclair Dunlop **A. Sinclair Dunlop**	Director	February 28, 2022
/s/ Alec Machiels **Alec Machiels**	Director	February 28, 2022
/s/ Stephanie M. O'Brien **Stephanie M. O'Brien**	Director	February 28, 2022
/s/ Paul Fonteyne **Paul Fonteyne**	Director	February 28, 2022

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.

SUMMARY OF NON-EMPLOYEE DIRECTOR COMPENSATION PROGRAM

Apellis Pharmaceuticals, Inc. (the "Company") will maintain the following non-employee director compensation program, effective January 1, 2022:

Cash Compensation.

Each non-employee director will receive a cash retainer for service on the board of directors (the "Board") and for service on each committee on which the director is a member. The chairmen of the Board and of each committee will receive higher retainers for such service. The amounts of the retainers are as follows:

	Member Annual Retainer	Chairman Additional Annual Retainer
Board of Directors	$ 45,000	$ 33,750
Audit Committee	$ 10,000	$ 20,000
Compensation Committee	$ 7,500	$ 15,000
Nominating and Corporate Governance Committee	$ 5,000	$ 10,000

These retainers are payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment shall be prorated for any portion of such quarter during which the director was not serving on the Board, on such committee or in such position.

The Company will also reimburse its non-employee directors for reasonable travel and other expenses incurred in connection with attending Board and committee meetings.

Equity Compensation.
Initial Stock Option Grant. Upon his or her initial election to the Board, each non-employee director will receive an option under the 2017 Plan to purchase the number of shares of Common Stock that has a Black Scholes value as of the date of the grant equal to $600,000 (as calculated using the same methodology that the Company then uses to calculate the value of stock awards for purposes of the Company's financial statements). Subject to the non-employee director's continued service as a director, such option will vest with respect to one-third of the shares on each of the first, second and third anniversaries of the grant date and, in the event of a change in control of the Company, the vesting schedule of the option will accelerate in full. The exercise price of the option will be equal to the fair market value of the Common Stock on the date of grant. Each option will have a seven year term from the date of grant.

Annual Stock Option Grant. Each non-employee director who has served on the Board for at least six months will receive, on January 1, 2022, a grant of an option under the 2017 Plan to purchase the number of shares of Common Stock that has a Black Scholes value as of the date of the grant equal to $200,000 (as calculated using the same methodology that the Company then uses to calculate the value of stock awards for purposes of the Company's financial statements). Unless otherwise provided at the time of grant, subject to the non-employee director's continued service as a director, the option will vest in four equal quarterly installments on April 1, July 1 and October 1 of the year in which the grant is made and on January 1 of the following year, and, in the event of a change in control of the Company, the vesting schedule of the option will accelerate in full. The exercise price of the option will be equal to the fair market value of the Common Stock on the date of grant. Each option will have a seven year term from the date of grant.

Annual Restricted Stock Unit Grant. Each non-employee director who has served on the Board for at least six months will receive, on January 1, 2022, restricted stock units for a number of shares of Common Stock determined by dividing $200,000 by the closing price of the Common Stock on the date of grant. Unless otherwise provided at the time of grant, subject to the non-employee director's continued service as a director, the restricted stock unit will

fully vest on the first anniversary of the date of grant, and, in the event of a change in control of the Company, the restricted stock unit will accelerate in full. Each grant may provide that the director may defer vesting until the termination of his or her service.

Acceleration of Vesting. All options and restricted stock units issued to the non-employee directors under the Company's non-employee director compensation program will become exercisable in full upon a change in control of the Company.

Apellis

Exhibit 10.29

6400 Westwind Way, Suite A
Crestwood, KY, 40014
P:(502) 241-4114

April 20, 2020

Nur Nicholson

VIA EMAIL

Dear Nur:

We are pleased to extend you an offer to join Apellis Pharmaceuticals, Inc. ("Apellis" or the "Company") as our Chief Technical Officer. You will be responsible for developing and executing our manufacturing, supply chain, and technical development strategy in support of our overall business plan and strategic direction. You will provide strategic leadership to ensure scalable and cost-efficient manufacturing for later stage and commercial products as well as meeting the needs of our development pipeline.

You will work from our offices in the Waltham area, with travel as may be reasonably required from time to time to properly fulfill your employment duties and responsibilities. You will report to the Chief Executive Officer.

Subject to satisfaction of the conditions described in this letter, you will begin employment on or before August 10, 2020 (or another mutually acceptable start date). You agree to devote your full business time, attention and commercially reasonable efforts to the performance of your duties and to the furtherance of the Company's interests, and during the period of your employment, shall not engage in any other employment, consulting or other business activity without the prior written consent of the Company. Any exceptions must be first approved in writing by the Chief Executive Officer after consultation with the Board of Directors.

Your initial annualized base salary will be $400,000, paid in accordance with our standard payroll practices and subject to all withholdings and deductions as required by law. You will also be eligible to participate in the 2020 Apellis Bonus Program with an annual target bonus of 40% of your annualized base salary, based upon company, departmental, and individual performance. You must remain employed with the Company through the date of the bonus payment to receive such payment. All bonus payments, if any, are subject

to the approval of the Board of Directors. Any bonus for fiscal year 2020, if any, will be pro-rated from your start date.

You will be eligible for our standard benefits package offered to every full-time employee, which includes health insurance, LTD/ADD/life insurance, and 401(k). You will be reimbursed for travel and other expenses in accordance with our reimbursement policy. You will be entitled to 20 days paid time off (PTO) for vacation, illness or personal business each full calendar year (i.e., accruing at the rate of 13.33 hours per month) in accordance with our PTO policy. Apellis reserves the right to amend, modify or terminate any of its benefit plans, policies or programs at any time and for any reason.

You will be eligible to receive separation benefits under the terms and conditions of our Executive Separation Benefits and Retention Plan, adopted on October 1, 2019 (the “Separation Benefits Plan”), a copy of which is provided for your reference. All forms of cash compensation paid to you as an employee pursuant to this offer letter or the Separation Benefits Plan shall be less all applicable withholdings.

You will be eligible for a one-time sign-on bonus in the amount of $75,000.00. This will be paid with your first payroll and subject to all withholdings and deductions as required by law. If you leave Apellis prior to your first anniversary you will be required to pay back this bonus in full, other than in the case of a reduction in force or termination by the Company without cause.

Subject to the approval of the Board of Directors, you will receive an option to purchase 125,000 shares of Common Stock at an exercise price equal to the fair market value as determined by the Board at the time of the grant, with such option to vest in equal monthly installments over four years from your date of employment, subject to a one-year vesting cliff. To the extent permitted under the Plan and the Internal Revenue Code, this option shall be an “incentive stock option” and otherwise will be treated as an “inducement grant” of non-statutory stock option in accordance with Nasdaq Listing Rule 5635(c)(4). The terms of these grants will be set forth in one or more stock option agreements and shall be subject to the provisions of the Separation Benefits Plan.

This offer letter is intended to comply with Section 409A of the Internal Revenue Code ("Section 409A") or an exemption thereunder and shall be construed and administered in accordance with Section 409A. Notwithstanding any other provision of this offer letter, payments provided under this offer letter may only be made upon an event and in a manner that complies with Section 409A or an applicable exemption. Any payments under this offer letter that may be excluded from Section 409A either as separation pay due to an involuntary separation from service or as a short-term deferral shall be excluded from Section 409A to the maximum extent possible. For purposes of Section 409A, any installment payment provided under this offer letter shall be treated as a separate payment. Any payments to be made under this offer letter upon a termination of employment shall only be made upon a "separation from service" under Section 409A. Notwithstanding the foregoing, the Company makes no representations that the

payments and benefits provided under this offer letter comply with Section 409A and in no event shall the Company be liable for all or any portion of any taxes, penalties, interest or other expenses that may be incurred by you on account of non-compliance with Section 409A. If any payment or benefit provided to you in connection with termination of employment is determined to constitute "nonqualified deferred compensation" and you are determined to be a "specified employee," in each case within the meaning of Section 409A, the Company agrees to negotiate with you in good faith to appropriately and lawfully modify the contractual terms relating to such payment or benefit.

On your first day of employment, you will be given additional information about our procedures, policies, and benefit programs. We will require you, as a condition of employment, to verify your right to work in the United States and to enter into the standard noncompetition, nondisclosure, and development agreement on your first day of employment.

By signing below, you represent that (i) your employment with the Company and your execution of this offer letter does not and will not violate or conflict with agreements you may have with any former employer and (ii) you have provided the Company with all written agreements that describe any continuing post-employment obligations to any former employer. Your employment will be at will, and this letter does not represent any guarantee of employment for any period. If you wish to resign from your employment with the Company, we request not less than 15 calendar days' written notice.

This offer letter, along with the stock option agreement, the non-solicitation, nondisclosure and development agreement and any benefit plans, constitute the complete agreement between you and the Company, contain all the terms of your employment, and supersede any prior agreements, representations or understandings (whether written, oral or implied) between you and the Company. The terms of this offer letter and the resolution of any disputes as to the meaning, effect, performance or validity of this offer letter or arising out of, related to, or in any way connected with, this offer letter, your employment with the Company or any other relationship between you and the Company (the "Disputes") will be governed by Massachusetts law, excluding laws relating to conflicts or choice of law. You and the Company agree to submit to the exclusive personal jurisdiction of the federal and state courts located in the Commonwealth of Massachusetts in connection with any dispute or any claim related to any dispute.

You will be eligible for the reimbursement of moving expenses (based on an approved relocation estimate) to relocate to Waltham, including up to 4 months of temporary housing or up to $20,000.00. You will be required to submit receipts in order to receive reimbursement. If you leave Apellis before you have completed 12 months of employment you will be required to return any monies paid to you for moving expense reimbursement.

This offer will expire at the close of business, on Thursday, April 23, 2020, unless accepted by you prior to that time. This offer is contingent upon the successful completion

of a background check and satisfactory reference check and upon your execution of the Non-Solicitation, Nondisclosure and Development Agreement.

We are excited at the prospect of your joining our team. Feel free to contact me if you have questions or if you need any additional information.

Sincerely,

/s/ Timothy Sullivan

Timothy Sullivan
Chief Financial Officer
Apellis Pharmaceuticals, Inc.

ACCEPTED AND AGREED:

/s/ Nur Nicholson

Name : Nur Nicholson

Date : 4/22/2022

Apellis

Exhibit 10.30

6400 Westwind Way, Suite A
Crestwood, KY, 40014
P:(502) 241-4114

November 16, 2018

Adam Townsend

VIA EMAIL

Dear Adam:

We are pleased to extend you an offer to join Apellis Pharmaceuticals as Chief Commercial Officer. Subject to satisfaction of the conditions described in this letter, you will begin employment on November 16, 2018 (or another mutually acceptable start date). You agree to devote your full business time, attention and commercially reasonable efforts to the performance of your duties and to the furtherance of the Company's interests, and during the period of your employment, shall not engage in any other employment, consulting or other business activity without the prior written consent of the Company. Any exceptions must be first approved in writing by the Chief Executive Officer after consultation with the Board of Directors.

You will work from our offices in the Waltham, Massachusetts area, with travel as may be reasonably required from time to time to properly fulfill your employment duties and responsibilities. Your job responsibilities will include overseeing the successful direction, planning, and execution all aspects of Apellis' commercial policies, objectives, and initiatives. This includes the development of life cycle marketing strategies, pre-launch development, commercialization, launch and maximization of approved products, recruitment, deployment and development of employees and the commercial success of the business globally, based on such annual targets as are agreed to by the Chief Executive Officer and you; and such other responsibilities as may be delegated to you by the Chief Executive Officer, all as may be modified from time to time by the Chief Executive Officer, so long as any such other responsibilities and modifications are consistent with the position of Chief Commercial Officer.

You will report to the Chief Executive Officer.

Your initial salary will be $31,667 per month, equivalent to an annualized base salary of $380,000, paid in accordance with our standard payroll practices and subject to all withholdings and deductions as require by law, for your full-time efforts, of at least 40 hours per week. Your base salary will be subject to upward adjustment as determined by the Board of Directors in its sole discretion. For calendar year 2019 and thereafter, you

will also be eligible for annual bonus compensation of up to 40% of your annualized base salary, based upon the achievement of performance goals established by the Board of Directors for the Company, the commercial department and you as an individual executive, after consultation with you. Except as otherwise provided herein, you must remain continuously employed with the Company through the date of the bonus payment to receive such payment.

You will be eligible for the standard benefits package offered to every full-time employee at your level, which currently includes health insurance, LTD/ADD/life insurance, and 401(k), provided that you are eligible under, and subject to all provisions of, the plan documents that govern those programs. You will be reimbursed for reasonable travel and other expenses incurred by you in performing your services to the Company in accordance with our reimbursement policy. You will be entitled to 20 days paid time off (PTO) for vacation, illness or personal business each full calendar year (i.e., accruing at the rate of 13.33 hours per month) in accordance with our PTO policy. Apellis reserves the right to amend, modify or terminate any of its benefit plans, policies or programs at any time and for any reason.

If your employment with the Company is involuntarily terminated for reasons other than “for Cause” or you have Good Reason to terminate your employment (each, as defined herein), then subject to your execution and nonrevocation of a release of claims substantially in the form annexed hereto, you will be eligible to receive continuation of your base annual salary for a period of time equal to six months from your termination of employment, payable in accordance with the Company’s normal payroll practices, commencing with the payroll period following the date on which such release of claims becomes fully effective and nonrevocable; provided however that such severance pay shall in all cases be fully paid no later than the last day of the calendar year following the year of your termination of employment, and, if you participate in the Company’s group insurance plans, the Company will provide you with a lump sum amount to cover COBRA premiums in an aggregate net amount equivalent to six months’ coverage, after deduction of all applicable taxes and withholdings. Notwithstanding the foregoing, if your employment is terminated for any reason within three months of your start date, the Company will have no obligation to provide such severance pay.

For the purposes of this letter agreement, the Incentive Stock Option Agreement and any other equity award as is hereafter granted to you, the term “for Cause” shall mean: (i) willful and continuing failure to perform your material duties following the provision of thirty (30) days prior written notice detailing such failure; (ii) willful failure to comply with any valid, material and legal directive of the Chief Executive Officer or the Board of Directors that is consistent with your duties as Chief Commercial Officer; (iii) willful engagement in dishonesty, illegal conduct or gross misconduct, which is in each case injurious to the Company; (iv) embezzlement, misappropriation or fraud; (v) conviction of or plea of guilty or nolo contendere to a crime that constitutes a felony (or state law equivalent) or a crime that constitutes a misdemeanor involving moral turpitude; (vi) violation of, or material failure to comply with, any material written policy of the Company; (vii) willful unauthorized disclosure of confidential information of the Company, as

provided in the Non-Competition, Non-Solicitation, Nondisclosure and Development Agreement dated November 16, 2018; or (viii) a material breach of any material obligation under this Agreement.

For the purposes of this letter agreement, the Incentive Stock Option Agreement and any other equity award as is hereafter granted to you, the term “Good Reason” shall mean any action on the part of the Company or a successor in interest not consented to in writing by you, having the following effect or effects: (A) a material diminution in your duties, authority or responsibilities; (B) a material reduction in your base salary, other than a reduction comparable to reductions generally applicable to similarly situated persons, so long as any such reduction does not exceed 10% of your base salary; (C) the Company’s requiring your ongoing and regular services to be performed at a location more than fifty (50) miles from the geographic location at which you were providing services before such requirement; or (D) the Company’s material breach of this letter agreement, the Incentive Stock Option Agreement and any other equity award as is hereafter granted to you. Notwithstanding the occurrence of any such event or circumstance, such occurrence shall not be deemed to constitute Good Reason unless (x) you give the Company’s Board of Directors and the Company’s Chief Executive Officer (or the Board of Directors and Chief Executive Officer of the Company’s successor in interest, if applicable) written notice specifying that such event or circumstance will give rise to a right of termination no more than 90 days after the initial existence of such event or circumstance, (y) such event or circumstance shall not have been cured within thirty (30) days following such written notice; and (z) you terminate your employment within forty-five (45) days after the end of the 30-day cure period and prior to such event or circumstance having been cured.

Subject to the approval of the Board of Directors, you will receive an option to purchase 375,000 shares of Common Stock at an exercise price equal to the fair market value as determined by the Board of Directors at the time of the grant, with such option to vest as to 25% of the underlying shares on the first anniversary of the Start Date and to vest as to the balance in equal monthly installments of 2.08% thereafter through the fourth anniversary of the Start Date.

The vesting under your option will accelerate in accordance with the “double trigger” vesting provision set forth in the Incentive Stock Option Agreement, where 100% of the unvested shares underlying the option shall vest if your employment is terminated by the Company for reason other than “for Cause” or you resign for Good Reason at any time during the 12 month period after a change of control event (as defined in the Incentive Stock Option Agreement). All forms of cash compensation paid to you as an employee pursuant to this offer letter shall be less all applicable withholdings.

This offer letter is intended to comply with Section 409A of the Internal Revenue Code ("Section 409A") or an exemption thereunder and shall be construed and administered in accordance with Section 409A. Notwithstanding any other provision of this offer letter, payments provided under this offer letter may only be made upon an event and in a manner that complies with Section 409A or an applicable exemption. Any payments under

this offer letter that may be excluded from Section 409A either as separation pay due to an involuntary separation from service or as a short-term deferral shall be excluded from Section 409A to the maximum extent possible. For purposes of Section 409A, any installment payment provided under this offer letter shall be treated as a separate payment. Any payments to be made under this offer letter upon a termination of employment shall only be made upon a "separation from service" under Section 409A. Notwithstanding the foregoing, the Company makes no representations that the payments and benefits provided under this offer letter comply with Section 409A and in no event shall the Company be liable for all or any portion of any taxes, penalties, interest or other expenses that may be incurred by you on account of non-compliance with Section 409A. If any payment or benefit provided to you in connection with termination of employment is determined to constitute “nonqualified deferred compensation” and you are determined to be a “specified employee,” in each case within the meaning of Section 409A, the Company agrees to negotiate with you in good faith to appropriately and lawfully modify the contractual terms relating to such payment or benefit.

On your first day of employment, you will be given additional information about our procedures, policies, benefit programs and more. By signing below, you represent that (i) your employment with the Company and this offer letter does not and will not violate or conflict with any obligations you may have to or any on your first day of employment, you will be given additional information about our procedures, policies, and benefit programs. We will require you, as a condition of employment, to verify your right to work in the United States and to enter into the Non-Competition, Non-Solicitation, Nondisclosure and Development Agreement on your first day of employment. The noncompetition and nonsolicitation covenants shall run during the term of your employment and for six months thereafter. You acknowledge that the offer of employment, the terms of employment set forth herein (specifically including the salary continuation upon a termination not for Cause or for Good Reason) and the equity award constitute adequate consideration for the covenants in the Non-Competition, Non-Solicitation, Nondisclosure and Development Agreement. You have the right to consult with your own legal counsel for at least ten days prior to signing the agreement containing these covenants.

By signing below, you represent that (i) your employment with the Company and your execution of this offer letter does not and will not violate or conflict with agreements you may have with any former employer and (ii) you have provided the Company with all written agreements that describe any continuing post-employment obligations to any former employer. Your employment will be at-will, and this letter does not represent any guarantee of employment for any period. If you wish to resign from your employment with the Company, we request not less than 15 calendar days’ written notice. This offer letter, along with the Incentive Stock Option Agreement, the Non-Competition, Non-Solicitation, Nondisclosure and Development Agreement and any benefit plans, constitute the complete agreement between you and the Company, contain all the terms of your employment, and supersede any prior agreements, representations or understandings (whether written, oral or implied) between you and the Company. The terms of this offer letter and the resolution of any disputes as to the meaning, effect, performance or validity

of this offer letter or arising out of, related to, or in any way connected with, this offer letter, your employment with the Company or any other relationship between you and the Company (the "Disputes") will be governed by Massachusetts law, excluding laws relating to conflicts or choice of law. You and the Company agree to submit to the exclusive personal jurisdiction of the federal and state courts located in the Commonwealth of Massachusetts in connection with any dispute or any claim related to any dispute. This offer of employment is contingent upon the successful completion of a background check and satisfactory reference check and upon your execution of the noncompetition, nondisclosure and development agreement.

Adam, we are excited at the prospect of your joining our team. If this letter correctly sets forth the terms under which you will be employed by the Company, please sign this letter in the space provided below and return it to me. If you do not accept this offer by Monday, November 19, 2018, this offer will be deemed revoked. Please let me know if you have any questions.

Sincerely,

/s/ Cedric Francois

Cedric Francois, M.D., Ph.D
Chief Executive Officer
Apellis Pharmaceuticals Inc.
(502) 295-4607
cedric@apellis.com

Your employment will be at will, and this letter does not represent any guarantee of employment for any period. This offer will expire at the close of business on Monday, November 19, 2018 unless accepted by you prior to that time.

ACCEPTED AND AGREED:

/s/ Adam Townsend

Name : Adam Townsend

Date : 11/16/2018

Exhibit 21.1

SUBSIDIARIES OF APELLIS PHARMACEUTICALS, INC.

Subsidiary	Jurisdiction of Incorporation or Organization
Apellis Australia Pty Ltd.	Australia
Apellis Bermuda Ltd.	Bermuda
Apellis Cayman Holdings Limited	Cayman Islands
APL DEL Holdings LLC	United States
APL DEL Holdings II, LLC	United States
Apellis Germany GmbH	Germany
Apellis France S.A.S.	France
Apellis Ireland Ltd.	Ireland
Apellis Netherlands, B.V.	Netherlands
Apellis Switzerland GmbH	Switzerland
Apellis U.K. Limited	United Kingdom
Apellis MA Securities Inc.	United States
APL Sales I, LLC	United States
APL PRG I, Corp.	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 Nos. 333-229876, 333-221528, 333-236708, 333-236710, and 333-253518 on Form S-8 of our reports dated February 28, 2022, 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 this Annual Report on Form 10-K for the year ended December 31, 2021.

/s/ Deloitte & Touche LLP

Boston, Massachusetts

February 28, 2022

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, 2021 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 28, 2022

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, 2021 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 28, 2022

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, 2021 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 28, 2022

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, 2021 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 28, 2022

By: /s/ Timothy E. Sullivan

Timothy E. Sullivan
Chief Financial Officer and Treasurer