2024 Annual Report

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, 2024

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. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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 28, 2024, 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 $4.2 billion.

The number of shares of the registrant's common stock, par value $0.0001 per share outstanding as of February 19, 2025 was 125,515,813.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A in connection with its 2025 Annual Meeting of Stockholders within 120 days of the end of the registrant's fiscal year ended December 31, 2024. 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 on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K, 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:

- the ongoing commercialization of EMPAVELI and SYFOVRE;
- 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 Sobi, or by any future collaborators, including the timing of initiation, dosing of patients, enrollment and completion of these trials and expectations regarding the anticipated results from these trials;
- our sales, marketing and distribution capabilities and strategies, including for the commercialization and manufacturing of EMPAVELI, SYFOVRE and any future products for which we receive marketing approval;
- the rate and degree of market acceptance of EMPAVELI, SYFOVRE and any future products for which we receive marketing approval;
- our ability to identify and develop current and future products or product candidates with significant clinical benefits and commercial potential;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates for current and future treatment indications in the U.S. and other jurisdictions;
- our current and any future collaborations for the development and commercialization of our current and future product candidates;
- including our collaborations with Sobi and Beam Therapeutics, Inc.;
- our intellectual property position and strategy;
- the sufficiency of our cash and cash equivalents and our expected revenues from sales of EMPAVELI and SYFOVRE to fund our projected operating expenses and capital expenditures to profitability;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- developments relating to our competitors and our industry; and
- the impact of 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, SYFOVRE 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 systemic pegcetacoplan in the context of the commercially available product in the United States for the treatment of adults with paroxysmal nocturnal hemoglobinuria, or PNH, and references to Aspaveli refer to systemic pegcetacoplan in the context of the commercially available product in the European Union for the treatment of adults with PNH who are anemic after treatment with a C5 inhibitor for at least three months in each case, and references to IC-MPGN refer to primary immune complex membranoproliferative glomerulonephritis, as more fully described herein. Unless otherwise stated or the context indicates otherwise, all references in this Annual Report on Form 10-K to "SYFOVRE (pegcetacoplan injection)" and "SYFOVRE" refer to intravitreal pegcetacoplan in the context of the commercially available product for which we received approval from the U.S. Food and Drug Administration in February 2023 for the treatment of geographic atrophy secondary to age-related macular degeneration, or GA, and the Therapeutic Goods Administration in Australia in January 2025 for the every-other-month treatment of adult patients with GA with an intact fovea and when central vision is threatened by GA lesion growth. 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, and we may never achieve or maintain profitability. Our net losses were $197.9 million, $528.6 million, and $652.2 million for the years ended December 31, 2024, 2023 and 2022, respectively. We have obtained marketing approval for EMPAVELI for the treatment of paroxysmal nocturnal hemoglobinuria, or PNH, in multiple jurisdictions, and SYFOVRE for the treatment of geographic atrophy secondary to age-related macular degeneration, or GA, in the United States and Australia.
- Our prospects depend upon the commercial success of SYFOVRE and EMPAVELI. If we are unable to successfully commercialize SYFOVRE and EMPAVELI for their approved indications or develop and obtain marketing approval for or successfully commercialize pegcetacoplan for C3 glomerulopathy, or C3G, primary immune complex membranoproliferative glomerulonephritis, or IC-MPGN, and other indications, either alone or through a collaboration, or if we experience significant delays in doing so, our business could be harmed. SYFOVRE is currently only approved in the United States and Australia. We cannot be certain that we will be able to obtain regulatory approval for, and successfully commercialize, SYFOVRE in additional jurisdictions.
- We or others may later discover that EMPAVELI or SYFOVRE is less effective than previously believed or causes safety issues that were not previously identified, which could compromise our ability, or that of our collaborators, to market the product. For example, a small number of patients treated with SYFOVRE in the real world have experienced retinal vasculitis, a severe form of intraocular inflammation. A change in the perception of the benefit/risk profile of SYFOVRE may reduce market acceptance of the product and our product revenues may be adversely affected.
- We expect to continue to incur significant expenses in the course of operating our business. If our cash and cash equivalents, and cash generated from sales of EMPAVELI and SYFOVRE, are not sufficient to fund our projected operating plans and capital expenditure requirements to profitability, we will need to obtain additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate product development programs or delay or reduce our commercialization efforts.
- Patients with PNH who were previously untreated may not start treatment with EMPAVELI or patients who are being treated for PNH with eculizumab, ravulizumab, or iptacopan may not switch to treatment with EMPAVELI. Patients with GA may not be diagnosed or seek treatment with SYFOVRE, may elect to be treated with a competitor treatment, or may fail to comply with the treatment regimen over the progression of the disease.
- If we are not able to maintain our agreements with wholesale distributors, specialty pharmacy providers, third party payors, pharmacy benefit managers and group purchasing organizations, or maintain our products on formularies, the market opportunity and revenue for our products may be adversely affected.
- EMPAVELI, SYFOVRE, or any other products 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 face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do. In GA, we face competition from avacincaptad pegol, which the FDA approved for the treatment of GA in August 2023. In PNH, we face competition from eculizumab, ravulizumab and iptacopcan. We also face potential competition in C3G from iptacopan, for which a supplemental new drug application, or sNDA, in C3G was submitted to the FDA in late 2024.
- We have incurred debt under our financing agreement with Sixth Street Lending Partners to buy out the SFJ Pharmaceuticals development liability. Our business may not generate cash flows from operations in the future that are sufficient to service our debt and support our growth strategies. If our cash and cash equivalents and cash generated from sales of EMPAVELI and SYFOVRE are not sufficient to fund our projected operating plans and capital expenditure requirements to profitability, we will need to obtain additional funding. If we are unable to raise capital when needed, we may be required to adopt one or more alternatives, such as obtaining additional capital on terms that may be onerous or highly dilutive, selling assets, or restructuring debt, and we could be forced to delay, reduce or eliminate product development programs, or delay or reduce our commercialization effort.
- The regulatory approval process is expensive, time consuming and uncertain and may prevent us or our collaborators such as Sobi from obtaining marketing approvals for systemic pegcetacoplan in indications other than PNH, intravitreal pegcetacoplan for indications other than GA or in jurisdictions other than the United States and Australia, 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, for intravitreal pegcetacoplan for GA in jurisdictions other than the United States and Australia or for any other product candidate that we develop in any jurisdiction.

- If clinical trials of any of our 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 contract with third parties for the manufacture, storage and distribution of commercial and clinical supply of EMPAVELI and SYFOVRE 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, SYFOVRE, or our product candidates or that such quantities may be acquired 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 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 that specifically recite the active component.

PART I

Item 1. Business.

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. We believe that this approach has the potential to effectively control diseases with high unmet need and that are driven by excessive complement activation. We currently have two marketed drugs that target C3, the central protein in the complement cascade: SYFOVRE (pegcetacoplan injection), approved by the U.S. Food and Drug Administration, or FDA, in February 2023 for the treatment of geographic atrophy secondary to age-related macular degeneration, or GA; and EMPAVELI (pegcetacoplan), approved by the FDA in May 2021 for the treatment of paroxysmal nocturnal hemoglobinuria, or PNH.

We believe SYFOVRE has the potential to be the standard of care for patients with GA, a disease that affects an estimated 1.5 million people in the United States. While we have exclusive, worldwide commercialization rights for intravitreal pegcetacoplan, we intend to focus our commercialization efforts in the U.S. and explore international expansion in select markets, including Australia, where we received marketing approval in January 2025. For the year ended December 31, 2024 and 2023, we generated $611.9 million and $275.2 million in U.S. net product revenue from sales of SYFOVRE. We are also developing a next-generation therapy by combining SYFOVRE treatment with APL-3007, which is a small interfering RNA, or siRNA, aimed at comprehensively blocking complement activity in the retina and the choroid. We plan to initiate a Phase 2 multi-dose trial in patients with GA in the second quarter of 2025.

We believe that EMPAVELI has the potential to be a best-in-class treatment for a range of indications with high unmet needs. We have exclusive U.S. commercialization rights for EMPAVELI, and our collaboration partner, Swedish Orphan Biovitrum AB (Publ), or Sobi, has exclusive ex-U.S. commercialization rights for systemic pegcetacoplan outside of the United States. For the years ended December 31, 2024 and 2023, we generated $98.1 million and $91.0 million, respectively, in U.S. net product revenue from sales of EMPAVELI for PNH and received $18.4 million and $10.0 million, respectively, in royalties from our collaboration partner, Swedish Orphan Biovitrum AB (Publ), or Sobi, which has exclusive ex-U.S. commercialization rights for systemic pegcetacoplan outside of the United States.

The next indications we are pursuing with EMPAVELI are C3 glomerulopathy, or C3G, and primary immune complex membranoproliferative glomerulonephritis, or IC-MPGN, which together affect an estimated 5,000 people in the United States. We submitted a supplemental new drug application, or sNDA, to the FDA in early 2025, following the positive results from the Phase 3 VALIANT trial investigating systemic pegcetacoplan in adolescent and adult patients with naive and post-transplant recurrence C3G and IC-MPGN that we reported in August 2024. Importantly, the VALIANT study demonstrated positive effects on the three key markers of disease at six months: a 68% reduction in proteinuria in C3G and IC-MPGN patients compared to placebo ($p < 0.0001$), the primary endpoint. Results were consistent across all subgroups, including disease type, age, and transplant status. Additionally, pegcetacoplan-treated patients achieved stabilization of kidney function (nominal $p=0.03$), as measured by estimated glomerular filtration rate, and a substantial proportion of patients achieved a reduction in C3c staining intensity (nominal $p<0.0001$). Data also demonstrated favorable safety and tolerability results, consistent with pegcetacoplan's established profile. Additionally, in February 2025, Sobi received validation for its indication extension application for C3G and IC-MPGN from the European Medicines Agency, or EMA.

We plan to initiate two new Phase 3 clinical trials with EMPAVELI in the second half of 2025 for the treatment of primary focal segmental glomerulosclerosis, or FSGS, and delayed graft function, or DGF. Both FSGS and DGF are both rare, severe nephrology conditions with no approved therapies and in which complement overactivation plays a significant role. Sobi is also leading the development of systemic pegcetacoplan for hematopoietic stem cell transplantation-associated thrombotic microangiopathy, or HSCT-TMA, in hematology under the collaboration.

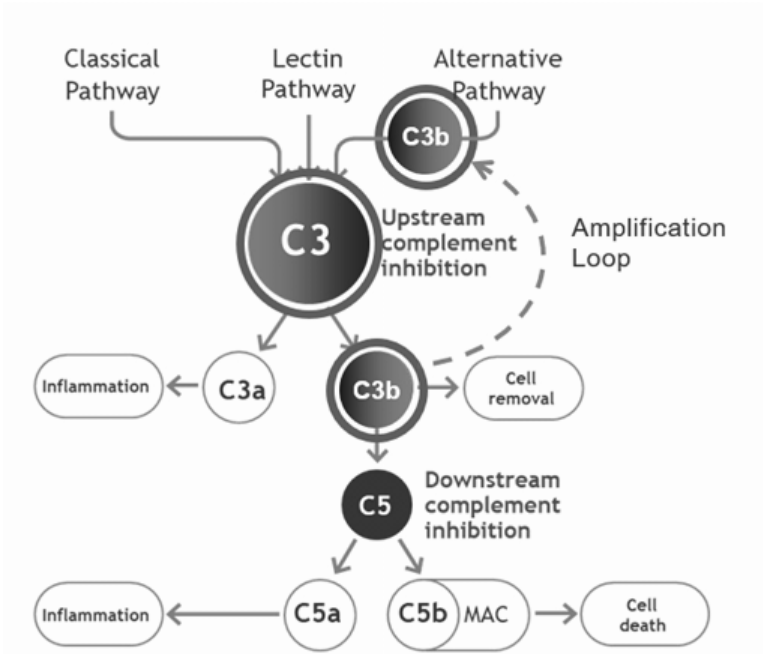
Finally, we are developing new product candidates to further advance our pipeline. Through our collaboration with Beam Therapeutics, Inc., or Beam, we have commenced pre-clinical studies for a treatment targeting the neonatal Fc receptor, orFcRn, which has the potential to be a first-in-class gene editing treatment for future target indications with one-time dosing. We are also developing other programs with our proprietary in-house capabilities.

Our Scientific 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 and become dysfunctional.

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 cell dysregulation and 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 cell opsonization by C3 fragments or C3a-mediated inflammation.

We have designed pegcetacoplan to target complement proteins centrally at the level of C3 and its fragment C3b. 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.

We are leveraging our expertise in complement immunology to develop new pipeline candidates that may affect different components or pathways within the complement system, whether as independent treatments or as a supplement to the effects of pegcetacoplan.

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 ophthalmology, rare disease, and neurology through the inhibition of the complement system.

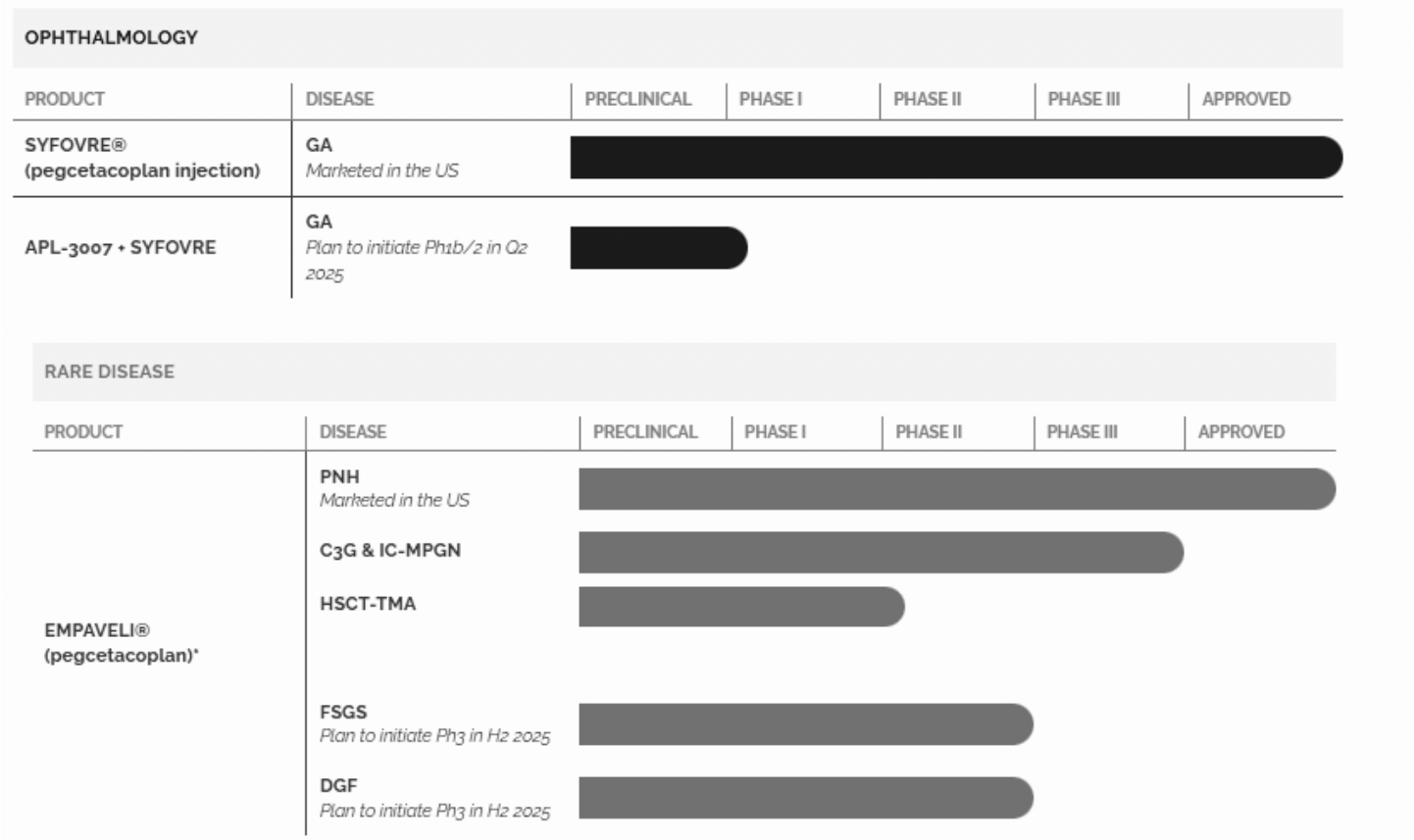
To achieve our goals, we are pursuing the following strategies in 2025 with a continued focus on compassion and commitment to patients:

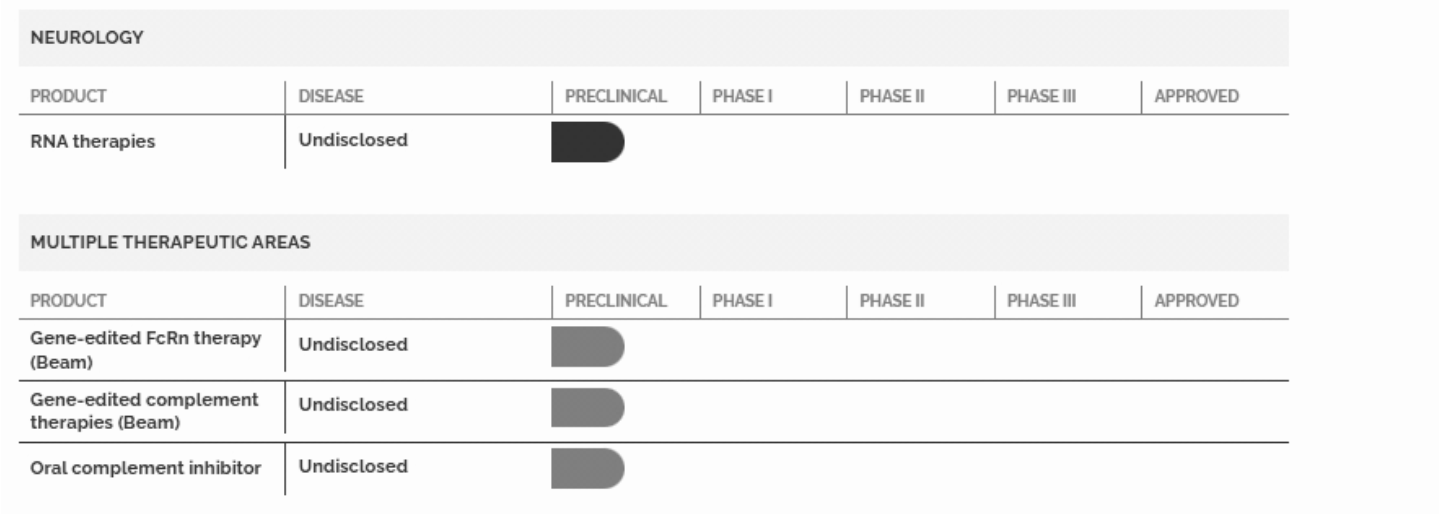
- Transform the treatment of GA with SYFOVRE.
- Maximize EMPAVELI's impact in rare diseases.
- Advance our innovative pipeline, leveraging our complement expertise.

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 products and our clinical programs:





Ophthalmology

We are commercializing SYFOVRE as a monotherapy for patients with GA.

Geographic Atrophy

GA is a type of 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 approximately 1.5 million people in the United States, are living with GA.

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

Because pegcetacoplan both blocks the production of C3a and C5a and prevents the accumulation of C3 fragments on retinal cells through the inhibition of C3, we believe that pegcetacoplan may control complement activation in the retinal environment to return 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.

Benefits of Our Approach

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

- *Prevention or reduction of the rate of retinal cell death, with increasing treatment effects over time*. We believe SYFOVRE may mitigate or prevent retinal cell death in GA, leading to a reduction in GA lesion growth over time. In our Phase 3 trials, SYFOVRE showed a slowing of GA progression, with evidence of treatment effects increasing over the 24-month period, and well-demonstrated safety profile following nearly 12,000 injections.
- *Treatment effects observed in two dosing regimens*. In our Phase 3 trials, SYFOVRE showed a slowing of GA progression over 24 months in both every-other-month and monthly dosing. The prescribing label for SYFOVRE indicates that the

recommended dose to be administered to each eye is once every 25 to 60 days. This provides physicians with flexibility to determine the appropriate dosing schedule for their individual patients.

- *Potential application to all patients with GA regardless of lesion location.* SYFOVRE, by targeting C3, has been designed to inhibit all three principal complement activation pathways and may therefore be effective in a broad patient population. In our Phase 3 trials at 24 months, pegcetacoplan showed a slowing of GA progression in lesions with or without subfoveal involvement. DERBY and OAKS are the only clinical trials to-date that have shown a slowdown in the progression of GA regardless of lesion location.

Regulatory Matters

In February 2023, the FDA approved intravitreal pegcetacoplan with the brand name SYFOVRE for the treatment of adult patients with GA secondary to AMD and, in January 2025, the Therapeutic Goods Administration, or TGA, in Australia, approved SYFOVRE for every-other-month treatment of adult patients with GA with an intact fovea where central vision is threatened by lesion growth.

We are currently evaluating our regulatory strategy for select jurisdictions outside the United States. In October 2024, we withdrew our marketing authorization application, or MAA, from the European Medicines Agency, or EMA, after the Committee for Medicinal Products for Human Use, or CHMP, adopted a negative opinion following the re-examination of the MAA, despite multiple dissenting votes by CHMP members. Despite our withdrawal, the European Commission issued a negative decision with respect to our MAA in December 2024.

Commercial and Medical Activities for GA

We launched SYFOVRE, the first approved treatment for GA, in the United States in March 2023. SYFOVRE is currently the market-leading treatment for GA, a disease that affects an estimated 1.5 million people in the United States.

Our U.S. field sales team has been engaging with eyecare professionals, or ECPs, focusing specifically on retina specialists and treating ophthalmologists. Field teams are focused on SYFOVRE brand messaging, highlighting key advantages such as increasing effects over time, its strong clinical profile, and dosing flexibility. We also have a thought leader liaison team, which is focused on building advocacy with key opinion leaders in the retina space, and a strategic account team, which identifies and develops working relationships with key decision makers within targeted private equity groups and large accounts. Our marketing efforts are designed to reach ECPs through digital and print media. We seek to reach patients through direct-to-consumer (TV, print and digital media) disease state education and branded SYFOVRE messaging encouraging them to see their eye doctor if they have symptoms or a previous diagnosis. Additionally, our efforts have focused on increasing awareness of GA and SYFOVRE with general ophthalmologists and optometrists to ensure GA patients are able to connect with a retina specialist or ophthalmologist who can treat them. We launched a practice finder tool to help physicians and patients identify practices near them that have recently treated GA.

Our market access team has been engaging with primary and secondary payers representing a significant percentage of GA patients. We have also established a robust distribution network by partnering with key specialty distributors and specialty pharmacies to maximize product access by retina specialists. Finally, we have a field reimbursement team to educate practices and address access issues to fully support the reimbursement journey for SYFOVRE.

ApellisAssist for SYFOVRE is designed to eliminate patient access barriers by providing enrolled individuals with insurance support, financial assistance for eligible patients, and education on the importance of maintaining treatment as prescribed. Additionally, prescribers have the option to enroll their patients in GAMyWay, our patient services program, for ongoing treatment support and continuous education.

Our medical affairs team is engaging with ECPs through our presence at medical meetings and other in-person engagements. Throughout 2024, we participated in key scientific meetings, including the American Academy of Ophthalmology, Retina Society, FLORETINA, and Macula Society.

Clinical Development

We are currently conducting two post-marketing studies: GALE and GARLAND. Our registrational Phase 3 DERBY and OAKS trials evaluated the efficacy and safety of SYFOVRE in patients with GA secondary to AMD. The DERBY and OAKS were initiated in September 2018, and we presented reported 24-month results from our DERBY and OAKS trials in August 2022, following 18-month results presented in March 2022 and 12-month results presented in September 2021. Prior to DERBY and OAKS, we completed the Phase 2 FILLY trial in August 2017.

Post-Marketing Studies

We are currently conducting a 36-month, open-label extension study (GALE) to evaluate the long-term safety and efficacy of intravitreal pegcetacoplan in patients with GA secondary to AMD. The objectives of the study are to evaluate the long-term incidence and severity of ocular and systemic treatment emergent adverse events as well as change in the total area of GA lesions as measured by fundus autofluorescence. Approximately 800 patients enrolled into the GALE extension study.

In February 2025, we presented data from GALE following four years of continuous treatment with SYFOVRE. Results showed that SYFOVRE continued to demonstrate increasing treatment effects over time.

We are currently conducting a 36-month, open label, Phase 4 study (GARLAND) to evaluate the safety, tolerability and treatment patterns of SYFOVRE in patients over the age of 60 with GA in a clinical practice setting. Secondary endpoints include GA progression, changes in drusen over time and the ability of physicians to determine GA lesion location. Approximately 234 patients have been enrolled into the GARLAND study.

Phase 3 Clinical Trials

Our Phase 3 clinical program in GA consisted of two prospective, multicenter, randomized, double-masked, sham-injection controlled trials (DERBY and OAKS) conducted at more than 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 received 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 received 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 compared to sham. The measurements of change in lesion size were analyzed at 12 months, 18 months, and 24 months. 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 analysis for the 24-month treatment period in August 2022. Monthly and every-other-month, or EOM, treatment with SYFOVRE showed increased effects over time. In OAKS, monthly and EOM treatment with SYFOVRE reduced GA lesion growth by 22% ($p<0.0001$) and 18% ($p=0.0002$), respectively. In DERBY, monthly and EOM treatment with SYFOVRE reduced GA lesion growth by 19% ($p=0.0004$) and 16% ($p=0.0030$), respectively. All p-values are nominal and were calculated using the same methodologies as the 12-month primary endpoint analysis.

Between months 18-24, the pegcetacoplan treatment effect accelerated compared to previous six-month periods, with robust reductions of GA lesion growth versus sham (all p-values are nominal). The increased effects were driven by a greater slowing of lesion growth by pegcetacoplan and not by an increase in the lesion growth rate in the sham group, which was highly consistent over each of the four six-month intervals (1.0+/-0.05 mm^2).

- DERBY: 36% monthly, $p<0.0001$; 29% EOM, $p=0.0002$
- OAKS: 24% monthly, $p=0.0080$; 25% EOM, $p=0.0007$

Additionally, the reduction of GA lesion growth in lesions without subfoveal involvement (28% monthly; 28% EOM) was comparable to the reduction in lesions with subfoveal involvement (34% monthly; 28% EOM) in the combined studies between months 18-24.

SYFOVRE was well-tolerated in both DERBY and OAKS, generally consistent with longer-term exposure to intravitreal injections. The most common adverse reactions (≥ 5%) reported in patients receiving SYFOVRE in these studies were ocular discomfort, neovascular AMD, vitreous floaters, and conjunctival hemorrhage. Rates of ischemic optic neuropathy events were higher in the monthly group as compared to the every-other-month and sham groups (1.7% of patients treated monthly, 0.2% of patients treated EOM and 0.0% of patients assigned to sham). Rates of endophthalmitis and intraocular inflammation were generally in line with those reported in studies of other intravitreal therapies. No events of occlusive or non-occlusive vasculitis or retinitis were observed over 24 months.

We used 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.

SYFOVRE and APL-3007

In January 2025, we shared Phase 1 data with APL-3007, our siRNA, in healthy volunteers showing greater than 90% knockdown of C3 as measured by the remaining levels of protein in the blood. Based on the results of this study, we are now developing a next generation treatment for GA by combining SYFOVRE plus APL-3007, which we believe may comprehensively block complement activity in the retina and the choroid. We believe that with less C3 present in the eye following administration with APL-3007, there may be a greater degree of efficacy contribution from SYFOVRE. We expect to initiate a Phase 2 study with SYFOVRE and APL-3007 in GA patients in the second quarter of 2025.

Product Development

We are developing a single package for SYFOVRE, or co-pack, that will contain SYFOVRE vials packaged with the necessary ancillaries for its administration. We expect that the co-pack will standardize administration of SYFOVRE and provide physicians with a more convenient way to store and handle the drug and ancillaries. The co-pack will also streamline both distribution operations and receipt by customers. We anticipate the supply of the co-pack to be available in the first half of 2026.

We are also developing a single dose, sterilized prefilled syringe for SYFOVRE. We believe the prefilled syringe will provide physicians with a new way to administer SYFOVRE that requires fewer steps compared to the current administration.

Rare Diseases

EMPAVELI in PNH

We launched EMPAVELI in the United States for patients with PNH following its approval by the FDA in May 2021. We believe that EMPAVELI elevated the standard of care for patients with PNH. We generated net product revenue from sales of EMPAVELI of $98.1 million during the year ended December 31, 2024.

Systemic pegcetacoplan was subsequently approved by the European Commission, the United Kingdom, Canada, Japan, Saudi Arabia and Australia.

Paroxysmal Nocturnal Hemoglobinuria (PNH)

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.

Commercialization

Our sales efforts are focused on the health care professionals, or HCPs, and key treatment centers, who have patients that continue to experience breakthrough hemolysis, have persistently low hemoglobin, high fatigue, and require transfusions despite being on C5 inhibitors.

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 have Apellis Assist, a patient-focused program specifically designed to assist patients with onboarding, product training and ongoing support with pegcetacoplan treatment, and we 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.

Our medical affairs team is engaging with physicians through our presence at medical meetings and other in-person engagements. In December 2024, we participated in the American Hematology Society, or ASH, annual meeting. Sobi will conduct medical affairs activities for systemic pegcetacoplan outside the United States.

Development

In June 2018, we initiated the Phase 3 PEGASUS trial in patients. 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, regardless of eculizumab dose or transfusion history. The primary efficacy endpoint of the trial was the change in hemoglobin level from baseline at week 16.

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.

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 ($p < 0.0001$). 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. In both the PEGASUS and PRINCE trials, the safety profile of systemic pegcetacoplan was comparable to eculizumab and consistent with previously reported data.

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. No unexpected safety concerns have been observed in patients in the clinical or post-marketing settings.

EMPAVELI in Nephrology

C3G glomerulopathy, or C3G, and primary immune complex membranoproliferative glomerulonephritis, or IC-MPGN, are rare, debilitating kidney diseases that affect an estimated 5,000 people in the United States, for which no therapies are currently approved. Symptoms of these diseases 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. Since pegcetacoplan is designed to prevent C3 activation, 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.

Regulatory Matters and Clinical Development

We submitted a sNDA to the FDA in early 2025 following the positive results from the Phase 3 VALIANT trial investigating EMPAVELI in adolescent and adult patients with naive and post-transplant recurrence C3G and IC-MPGN. EMPAVELI received orphan drug designation from the FDA for the treatment of C3G in December 2018. In February 2025, Sobi received EMA validation for its indication extension application for C3G and primary IC-MPGN in the European Union.

In August 2024, we announced positive results from our VALIANT study, a randomized, placebo-controlled, double-blinded, multi-center Phase 3 trial in 124 patients who are 12 years of age and older with C3G or primary IC-MPGN. The VALIANT study demonstrated positive effects on the three key markers of disease at Week 26: a 68% reduction in proteinuria in pegcetacoplan-treated patients compared to placebo ($p<0.0001$), the primary endpoint. Results were consistent across all subgroups, including disease type, age, and transplant status. Additionally, pegcetacoplan-treated patients achieved stabilization of kidney function (nominal $p=0.03$), as

measured by estimated glomerular filtration rate, and a substantial proportion of patients achieved a reduction in C3c staining intensity (nominal p<0.0001). Pegcetacoplan also demonstrated favorable safety and tolerability results, consistent with its established profile.

In October 2023, we announced positive results from our NOBLE trial, a randomized, placebo-controlled Phase 2 trial in post-transplant recurrence of C3G and IC-MPGN. Specifically, at 12 weeks, 80% of patients showed a reduction in C3c staining by one or more orders of magnitude of intensity from baseline, the primary endpoint, and 40% of patients showed zero staining intensity, indicating that C3c deposits were cleared. Patients also showed improvements across key clinical measures, including a mean reduction in proteinuria, and stabilized kidney function. There were no discontinuations due to treatment-emergent adverse events.

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.

We plan to initiate two pivotal studies with EMPAVELI in FSGS and DGF in the second half of 2025. Complement plays a significant role in both diseases, and there are currently no FDA-approved therapies. FSGS is a rare kidney disease that causes scarring in the glomeruli and, similar to C3G and IC-MPGN, results in end stage kidney disease within 5-10 years for approximately half of patients. There are an estimated 13,000 primary FSGS patients in the United States. DGF is a complication in kidney transplantation where the transplanted kidney fails to function and typically requires dialysis within the first week of transplant. This negatively affects the long-term survival of the kidney and overall patient outcomes. In 2023, there were an estimated 21,000 transplants in the U.S. using deceased donor kidneys, of which DGF occurred in 30-35% of them.

EMPAVELI in Other Indications

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. 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. The Phase 2 trial is an open label, single arm, multicenter trial evaluating the pharmacokinetics, efficacy and safety and tolerability of pegcetacoplan in approximately 12 patients with HSCT-TMA. Sobi expects to report top-line on this study in mid-2025.

Beam Research Collaboration

In June 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. We have commenced pre-clinical studies for a FcRn treatment, which has the potential to be a first-in-class gene editing treatment for future target indications with one-time dosing.

Collaboration and License Agreement with Sobi

On October 27, 2020, we and our subsidiaries, Apellis International GmbH (f/k/a Apellis Switzerland GmbH) and APL DEL Holdings, LLC, entered into a Collaboration and License Agreement (the "Sobi 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").

Under the Sobi collaboration agreement, we 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.

We retain 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 Sobi collaboration agreement, we and Sobi agreed to collaborate to develop Licensed Products for certain indications, including PNH, C3G, IC-MPGN and HSCT-TMA, and any other indications subsequently agreed upon by the parties, for commercialization by or on behalf of us 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, 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.

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

We agreed to 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 Sobi 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.

We 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 Sobi collaboration agreement, we remain responsible for its license fee obligations (including royalty obligations) to the Trustees of the University of Pennsylvania ("Penn"), as a licensor of Apellis.

We received $18.4 million in royalties from Sobi during the year ended December 31, 2024 and $10.0 million in royalties from Sobi in the year ended December 31, 2023.

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. 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 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

In June 2021, we entered into an exclusive five-year research collaboration (the "Beam collaboration agreement") with Beam focused on the use of Beam's proprietary base editing technology to discover new treatments for complement-driven diseases. We 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 Beam collaboration agreement, we are 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 Beam 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. We 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 us with respect to any one program licensed under the Beam collaboration agreement and upon such election any license agreement in place at that time, would be terminated.

As part of the Beam collaboration agreement, we paid $50.0 million up-front, non-refundable payment to Beam in July 2021 and $25.0 million in June 2022. We and Beam are each 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 us, as well as royalty payments on sales. The Beam collaboration agreement has an initial term of five years and may be extended up to two years on a per year 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, 2024, we own a total of 27 U.S. patents and 35 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 is an analog of the cyclic peptide compstatin, based on technologies that we have developed internally or have exclusively licensed from 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. Seven 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. 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. Eight of our U.S. patents are listed for SYFOVRE in the FDA's Orange Book. 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 would have terms extending into 2040. In addition, we own patent families relating to use of pegcetacoplan for the treatment of PNH or for the treatment of GA that have terms extending into 2041 through 2043.

In addition to the technology that we developed internally relating to compstatin analogs, we hold exclusive licenses from Penn. 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 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, small molecule, and protein-based approaches. The filings cover, for example, the composition of matter of certain of our product candidates and methods of use for treating particular complement-mediated disorders. Patents issuing based on these applications would have terms extending into 2041 through 2044.

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 have an exclusive license from Beam to this intellectual property to the extent it specifically covers 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, and we have applied for and will continue to apply for such extensions in jurisdictions in which pegcetacoplan is approved. In the future, if and when our product candidates 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 to our wholly owned subsidiaries, APL DEL Holdings, LLC and Apellis International GmbH (f/k/a 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)

We are party to 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. 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 pegcetacoplan, 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 were obligated to make a $0.1 million 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 $1.7 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, and to pay low single-digit royalties to Penn based on net sales of each licensed product by us and our affiliates and sublicensees and specified minimum quarterly royalty thresholds. In addition, we are obligated to pay Penn a specified portion of income we receive from sublicensees.

Our royalty obligation with respect to each licensed product in a country extends until the later of the expiration of the last-to-expire patent licensed from Penn covering the licensed product in the country or the expiration of a specified number of years after the first commercial sale of the licensed product in the country. As of December 31, 2024 and 2023, respectively, we have incurred royalty expense of $6.4 million and $4.8 million on sales of EMPAVELI and Aspaveli.

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.

In January 2021, we paid $25.0 million for a sublicense fee owed to Penn related to the Sobi collaboration agreement and another licensing transaction. In August 2021, we paid $1.0 million to Penn upon the achievement of a development milestone, net of a credit for the annual license maintenance payment. In June 2022, we paid an additional $5.0 million to Penn upon the achievement of a development milestone. In January 2023, we paid $1.0 million to Penn upon the achievement of a sales milestone for EMPAVELI in 2022. In January 2024, we paid $0.5 million for a sublicense fee owed to Penn related to Sobi obtaining regulatory approval in Japan. Additionally, in January 2024, we paid $1.5 million as a result of the achievement of a sales milestone for EMPAVELI and Aspaveli.

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

We are party to 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 the treatment of ophthalmic indications. Three of the licensed patents are listed for SYFOVRE in the FDA's orange book. We have the right to grant sublicenses under the license.

Under the license agreement, we were obligated to make a $0.1 million 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 $3.2 million based on achieving specified development and regulatory approval milestones, including $2.3 million upon approval of an NDA, and up to $5.0 million based on achieving specified annual sales milestones with respect to each licensed product, and to pay low single-digit

royalties to Penn based on net sales of each licensed product by us and our affiliates and sublicensees and specified minimum quarterly royalty thresholds. In addition, we are obligated to pay Penn a specified portion of income we receive from sublicensees.

In April 2023, the Company paid $2.3 million for the achievement of a regulatory milestone as a result of the FDA approval of SYFOVRE in February 2023. In 2023, the Company incurred $5.0 million as a result of the achievement of sales milestones for SYFOVRE of which the Company paid $2.0 million in October 2023 and the remaining $3.0 million in January 2024.

As of December 31, 2024 and 2023, respectively, we have incurred royalty expense of $19.8 million and $8.9 million as a result of sales of SYFOVRE

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 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. In August 2023, Astellas Pharma Inc. received FDA approval for avacincaptad pegol, a C5 inhibitor, for the treatment of GA. We are aware of other 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 3 clinical trials; pozelimab, an anti-C5 antibody developed by Regeneron Pharmaceuticals Inc. in combination with cemdisiran, an RNAi therapeutic targeting C5 developed by Alnylam Pharmaceuticals, Inc., in Phase 3 clinical trials; JNJ1887 , an intravitreal gene therapy targeting CD59 being developed by The Janssen Pharmaceutical Companies of Johnson & Johnson in Phase 2 clinical trials; AVD104, a glycan-coated nanoparticle targeting macrophage and complement factor H, being developed by Aviceda Therapeutics, Inc. in Phase 2 clinical trials; BI 771716, a C3 antibody fragment being developed by Boehringer Ingelheim Pharmaceuticals, Inc. in Phase 2 clinical trials; and other product candidates that do not target the complement system that are either in a single Phase 3 or in Phase 2 clinical trials, including but not limited to therapies being developed by Stealth BioTherapeutics, Inc., Belite Bio, Inc., Lineage Cell Therapeutics, Inc. (in collaboration with Roche/Genentech), Boehringer Ingelheim Pharmaceuticals, Inc., ONL Therapeutics, Inc., and Ocugen Inc. Novartis has initiated a Phase 2 trial of orally administered iptacopan, a factor B inhibitor, in patients with early or intermediate AMD.

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 marketed by AstraZeneca. The FDA approved danicopan as an add-on treatment to eculizumab and ravulizumab in April 2024. In December 2023, the FDA approved iptacopan, which is marketed by Novartis AG, or Novartis, for the treatment of adults with PNH. Iptacopan is an oral, Factor B inhibitor of the alternative complement pathway. The FDA approved crovalimab, an anti-C5 antibody developed by Roche and Chugai Pharmaceutical Co, in the United States in June 2024.

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 pozelimab + cemdisiran, currently in Phase 3 clinical trials, and as other products in early stages of development.

Amgen Inc. developed ABP959, a biosimilar for eculizumab, which has been approved in the European Union, as has Epysgli from Samsung Bioepis. 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.

C3G. There are currently no approved drugs for C3 glomerulopathy. There are treatments in clinical development, including iptacopan being developed by Novartis, which is currently under review with the FDA; OMS906, a MASP-3 inhibitor monoclonal antibody being developed by Omeros Corp., in a Phase 2 trial; KP104, an anti C5-Factor H bifunctional protein being developed by Kira Pharmaceuticals, currently in a Phase 2 renal basket trial; and ARO-C3, an RNAi to reduce C3 production developed by Arrowhead Pharmaceuticals, currently in a Phase 1/2 renal basket trial.

IC-MPGN. There are currently no approved drugs for IC-MPGN. There are potential treatments in clinical development, including iptacopan being developed by Novartis, currently in Phase 3 clinical trials, and OMS906, a MASP-3 inhibitor monoclonal antibody being developed by Omeros Corp., in a Phase 2 clinical trial.

HSCT-TMA. Currently there are three treatments in late-stage clinical development: ravulizumab, developed by AstraZeneca, nomacopan being developed by Akari, and narsoplimab, being developed by Omeros, are all in Phase 3 trials.

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 and SYFOVRE in the United States and plan to conduct commercial development for EMPAVELI in the United States if it is approved in other indications. Sobi has global co-development and exclusive ex-U.S. commercialization rights for Aspaveli. We plan to conduct commercial development for intravitreal pegcetacoplan in select countries outside of the U.S. 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.

For EMPAVELI and SYFOVRE 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 and GA, have built our field market access team and our sales team.

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 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 products, product candidates and other product candidates that we may develop in the future.

The process for manufacturing our products and 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 believe the costs associated with manufacturing drug product for our products and product candidates is 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, and a commercial supply agreement with NOF Corporation, or NOF, to purchase activated polyethylene glycol derivative, or PEG, which is

a component of pegcetacoplan. We also have a separate supply agreement for the manufacture of the drug product for each of EMPAVELI and SYFOVRE.

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

In December 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 systemic pegcetacoplan and intravitreal pegcetacoplan.

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.

The initial term of the Bachem Agreement continues until December 31, 2025. Thereafter, unless terminated earlier, the Bachem Agreement will automatically renew for an additional two-year term. 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

In March 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 each of systemic pegcetacoplan and intravitreal 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 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. In September 2024, we terminated the minimum purchase obligation with NOF for 2025. As a result of this termination, we incurred an expense of $6.4 million, which is included in Cost of Sales on the consolidated statements of operations and comprehensive loss income. As the amount is not due until January 2026, it is included in Other Liabilities on the consolidated balance sheet as of December 31, 2024.

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, Approval and Regulation of Drug Products 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 a 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. A company, institution or organization which takes responsibility for the initiation and management of a clinical development program for such products is referred to as a sponsor. A sponsor seeking approval to market and distribute a new drug or biologic product in the United States must typically secure 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 investigational new drug application, or IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, 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 for a new drug product, or a sNDA for a change to a previously approved drug product, which includes not only the results of the clinical trials, but also, detailed information on the chemistry, manufacture and quality controls for the product candidate and proposed labeling for one or more proposed indication(s);
- 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 application and program fees pursuant to the Prescription Drug User Fee Act, or PDUFA;
- securing FDA approval of the NDA or sNDA authorizing marketing of the drug product for particular indications in the United States; 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 a sponsor 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. These studies are generally referred to as IND-enabling studies. 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, sponsors 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 assure the safety and rights of patients and to help assure that the quality of the investigation will be adequate to permit an evaluation of the proposed drug's effectiveness and safety. 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.

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.

Once an IND application takes effect, the sponsor of the IND may amend the application as needed to ensure that the clinical trials are conducted according to protocols included in the IND. The FDA has indicated that sponsors are expected to submit amendments for new protocols or changes to existing protocols before implementation of the respective changes. New studies may begin, however, when the sponsor has submitted the change to the FDA for its review and the new protocol or changes to the existing protocol have been approved by the IRB with the responsibility for review and approval of the studies.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data monitoring 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.

Clinical Studies Outside the United States in Support of FDA Approval

Sponsors frequently conduct clinical trials at sites outside the United States. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, the studies must be conducted in accordance with GCP, including undergoing review and receiving approval by an independent ethics committee, or IEC, and seeking and receiving informed consent from subjects. GCP requirements 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.

The acceptance by the FDA of study data from clinical trials conducted outside the United States in support of US approval may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials are subject to the applicable local laws of the foreign jurisdictions where the trials are conducted.

Reporting Clinical Trial Results

Under 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, or 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.

The PHSA grants the Secretary of Health and Human Services, or HHS, 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. Violations may also result in injunctions and/or criminal prosecution or disqualification from federal grants.

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, or 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.

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. A development safety update report detailing the results of the clinical trials must be submitted annually to the FDA. 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 five 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. A Type D meeting is focused on a narrow set of issues (should be limited to no more than 2 focused topics) and should not require input from more than 3 disciplines or divisions. Finally, INTERACT meetings are intended for novel products and development programs that present unique challenges in the early development of an investigational product.

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. The PREVENT Pandemics Act, which was enacted in December 2022, clarifies that foreign drug manufacturing establishments are subject to registration and listing requirements even if a drug or biologic undergoes further manufacture, preparation, propagation, compounding, or processing at a separate establishment outside the United States prior to being imported or offered for import into the United States.

Pediatric Studies

Under the Pediatric Research Equity Act, or 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, or 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 sponsor 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 a sponsor, 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 sponsor, 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. The FDA is required to send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. It further requires the FDA to publicly post the PREA Non-Compliance letter and the sponsor's response.

Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation intended for a non-cancer indication, although the 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. Further, Section 505B of the FDCA, as amended by the FDA Reauthorization Act of 2017, or FDARA, requires that any original NDA or BLA submitted on or after August 18, 2020, for a new active ingredient, must contain reports on the molecularly targeted pediatric cancer investigation, unless the requirement is waived or deferred, if the drug that is the subject of the application is: (i) intended for the treatment of an adult cancer, and (ii) directed at a molecular target that the Secretary of HHS determines to be substantially relevant to the growth or progression of a pediatric cancer in accordance with FDA guidance. The FDA also maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population. In May 2023, the FDA issued new draft guidance that further describes the pediatric study requirements under PREA.

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.

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.

With the passage of FDORA, Congress modified certain provisions governing accelerated approval of drug and biologic products. Specifically, the new legislation authorized the FDA to require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded and to submit progress reports on its post-approval studies to FDA every six months until the study is completed. Moreover, FDORA established expedited procedures authorizing FDA to withdraw an accelerated approval if certain conditions are met, including where a required confirmatory study fails to verify and describe the predicted clinical benefit or where evidence demonstrates the product is not shown to be safe or effective under the conditions of use. The FDA may also use such procedures to withdraw an accelerated approval if a sponsor fails to conduct any required post-approval study of the product with due diligence, including with respect to "conditions specified by the Secretary." The new procedures include the provision of due notice and an explanation for a proposed withdrawal, and opportunities for a meeting with the Commissioner or the Commissioner's designee and a written appeal, among other things.

In March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. The agency indicated that the accelerated approval pathway is commonly used for approval of oncology drugs due to the serious and life-threatening nature of cancer. Although single-arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust efficacy and safety assessment and allows for direct comparisons to an available therapy. To that end, the FDA outlined considerations for designing, conducting, and analyzing data for trials intended to support accelerated approvals of oncology therapeutics. Subsequently, in December 2024 and January 2025, the FDA issued additional draft guidances relating to accelerated approval. These guidances describe the FDA's views on what it means to conduct a confirmatory trial with due diligence and how the agency plans to interpret whether such a study needs to be underway at the time of approval. While these guidances are currently only in draft form and will ultimately not be legally binding even when finalized, sponsors typically observe the FDA's guidance closely to ensure that their investigational products qualify for accelerated approval.

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 PDUFA is substantial (for example, for federal fiscal year 2025 this application fee is $4,310,002), and the sponsor of an approved application is also subject to an annual program fee, currently set at $403,889 per eligible prescription product for federal fiscal year 2025. 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 sponsor 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, or RTF, determination to the sponsor. 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 sponsor 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 sponsor 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. With passage of the FDORA, Congress clarified the FDA's authority to conduct inspections by expressly permitting inspection of facilities involved in the preparation, conduct, or analysis of clinical and non-clinical studies submitted to FDA as well as other persons holding study records or involved in the study process. To ensure cGMP and GCP compliance by its employees and third-party contractors, a sponsor may incur significant expenditure of time, money and effort in the areas of training, record keeping, production and quality control.

Moreover, the FDA will review a sponsor's financial relationship with the principal investigators who conducted the clinical trials in support of the NDA. That is because, under certain circumstances, principal investigators at a clinical trial site may also serve as scientific advisors or consultants to a sponsor and receive compensation in connection with such services. Depending on the level of that compensation and any other financial interest a principal investigator may have in a sponsor, the sponsor may be required to report these relationships to the FDA. The FDA will then evaluate that financial relationship and determine whether it creates a conflict of interest or otherwise affects the interpretation of the trial or the integrity of the data generated at the principal investigator's clinical trial site. If so, the FDA may exclude data from the clinical trial site in connection with its determination of safety and efficacy of the investigational product.

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 sponsor 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 NDA 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. Although the FDA has not yet finalized that guidance, the agency did issue draft guidance in September 2023 that outlines considerations for relying on confirmatory evidence in lieu of a second clinical trial to demonstrate efficacy.

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, or 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 sponsor 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 sponsor 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. CRLs are not publicly available documents.

In the event that a sponsor wishes to make a change to a product that has been approved under an NDA, the sponsor must submit an sNDA to the FDA. Such changes may include a revision of the labeling for the approved product, addition of a new indication, a change in the dosage, strength or formulation of the drug product, or a modification of the manner in which the drug is manufactured. Under the timelines established pursuant to PDUFA, the standard review time for an sNDA is generally 10 months from receipt of the application by the FDA.

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. Moreover, with passage of the Pre-Approval Information Exchange Act in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. Previously, such communications were permitted under FDA guidance, but the new legislation explicitly provides protection to sponsors who convey certain information about products in development to payors, including unapproved uses of approved products. In addition, in October 2023, the FDA published draft guidance outlining the agency's non-binding policies governing the distribution of scientific information on unapproved uses to healthcare providers. This draft guidance calls for such communications to be truthful,

non-misleading, factual, and unbiased and include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use.

In addition, in January 2025, the FDA published final guidance outlining its policies governing the distribution of scientific information to healthcare providers about unapproved uses of approved products. The final guidance calls for such communications to be truthful, non-misleading and scientifically sound and to include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use of the approved product. If a company engages in such communications consistent with the guidance's recommendations, the FDA indicated that it will not treat such communications as evidence of unlawful promotion of a new intended use for the approved product.

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 HHS, 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, or 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, or 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 sponsor 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 sponsor for approval of the application "were not conducted by or for the sponsor and for which the sponsor 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 sponsor. 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) sponsor can establish that reliance on the FDA's previous approval is scientifically appropriate, the sponsor 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) sponsor.

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, the sponsor 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 abbreviated new drug application, or 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 regulatory exclusivity for the RLD has expired. The FDCA provides a period of five years of regulatory 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 sponsor may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of regulatory 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 sponsor 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 patents 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 sponsor'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 sponsor files its application with the FDA, the sponsor 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 sponsor is not seeking approval. To the extent that the Section 505(b)(2) sponsor is relying on studies conducted for an already approved product, the sponsor 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 sponsor would.

Specifically, the sponsor 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 sponsor 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 sponsor is not seeking approval).

If the ANDA sponsor has provided a Paragraph IV certification to the FDA, the sponsor 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 sponsor.

To the extent that the Section 505(b)(2) sponsor is relying on studies conducted for an already approved product, the sponsor 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 sponsor 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) sponsor.

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 exclusivity to the term of any existing unexpired patent or regulatory exclusivity, including the orphan drug exclusivity, for drug products. 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) sponsor 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.

In September 2021, the Court of Appeals for the 11th Circuit held that, for the purpose of determining the scope of market exclusivity, the term "same disease or condition" in the statute means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Thus, the court concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the "indication or use." Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, the FDA announced that, in matters beyond the scope of that court order, the FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved.

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 2025, the standard fee is $540,783 and the small business fee is $135,196.

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.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the Quality System Regulation, which covers the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging, and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the United States.

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.

Federal and State Data Privacy Laws

There are multiple privacy and data security laws that may impact our business activities, in the United States and in other countries where we conduct business or trials or where we may do business in the future. These laws are evolving and may increase both our obligations and our regulatory risks in the future. In the health care industry generally, under the Health Insurance Portability and Accountability Act of 1996, or HIPAA, the HHS has issued regulations to protect the privacy and security of protected health information, or PHI, used or disclosed by covered entities including certain healthcare providers, health plans, and healthcare clearinghouses. HIPAA also regulates standardization of data content, codes, and formats used in healthcare transactions and standardization of identifiers for health plans and providers. HIPAA also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. HIPAA may apply to us in certain circumstances and may also apply to our business partners in ways that may impact our relationships with them. Our clinical trials are regulated by the Common Rule, which also includes specific privacy-related provisions. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that may be applicable to our business. In addition to possible federal civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. State attorneys general also have authority to enforce state privacy and security laws. New laws and regulations governing privacy and security may be adopted in the future as well.

In 2018 California passed into law the California Consumer Privacy Act, or CCPA, which took effect on January 1, 2020, and imposed many requirements on businesses that process the personal information of California residents. Many of the CCPA's requirements are similar to those found in the General Data Protection Regulation, or GDPR, including requiring businesses to provide notice to data subjects regarding the information collected about them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA also affords California residents the right to opt-out of "sales" of their personal information. The CCPA contains significant penalties for companies that violate its requirements. In November 2020, California voters passed a ballot initiative for the California Privacy Rights Act, or CPRA, which went into effect on January 1, 2023, and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities.

In addition to California, several other states have passed comprehensive privacy laws similar to the CCPA and CPRA. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data (which includes health data in some cases). Some of the provisions of these laws may apply to our business activities. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under such laws, it is possible that some of our current or future business activities, including certain clinical research, sales and marketing practices, and the provision of certain items and services to our customers, could be subject to challenge under one or more of such privacy and data security laws. The heightening compliance environment and the need to build and maintain robust and secure systems to comply with different privacy compliance and/or reporting requirements in multiple jurisdictions could increase the possibility that a healthcare company may fail to comply fully with one or more of these requirements. If our operations are found to be in violation of any of the privacy or data security laws or regulations described above that are applicable to us, or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil, and administrative penalties, damages, fines, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a consent decree or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. We are subject to similar foreign laws to the extent our products are sold in foreign countries.

Review and Approval of Drug Products in the European Union

In addition to regulations in the United States, we are 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, or the 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.

Non-clinical Studies

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical (pharmaco-toxicological) studies must be conducted in compliance with the principles of GLP, as set forth in EU Directive 2004/10/EC (unless otherwise justified for certain particular medicinal products – e.g., radio-pharmaceutical precursors for radio-labeling purposes). In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical Trial Approval

On January 31, 2022, the new Clinical Trials Regulation (EU) No 536/2014, or CTR, became effective in the European Union and replaced the prior Clinical Trials Directive 2001/20/EC. The new CTR aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the European Union. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one EU Member State will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a new clinical trials portal overseen by the EMA and available to clinical trial sponsors, competent authorities of the EU Member States, and the public.

The CTR did not change the preexisting requirement that a sponsor must obtain prior approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the sponsor may only start a clinical trial at a specific clinical site after the applicable ethics committee has issued a favorable opinion.

The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive, or CTD, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the CTD remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR.

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, a sponsor 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, a sponsor must submit a 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 CHMP, established at the 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 sponsor 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 sponsors 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, a sponsor 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 sponsor 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.

Conditional Approval

In particular circumstances, EU legislation (Article 14–a Regulation (EC) No 726/2004 (as amended by Regulation (EU) 2019/5 and Regulation (EC) No 507/2006 on Conditional Marketing Authorizations for Medicinal Products for Human Use) enables sponsors to obtain a conditional marketing authorization prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional approvals may be granted for product candidates (including medicines designated as orphan medicinal products) if (1) the product candidate is intended for the treatment, prevention, or medical diagnosis of seriously debilitating or life-threatening diseases; (2) the product candidate is intended to meet unmet medical needs of patients; (3) a marketing authorization may be granted prior to submission of comprehensive clinical data provided that the benefit of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required; (4) the risk-benefit balance of the product candidate is positive, and (5) it is likely that the sponsor will be in a position to provide the required comprehensive clinical trial data. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

Exceptional Circumstances

Marketing authorization may also be granted "under exceptional circumstances" when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. This may arise in particular when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. This marketing authorization is close to the conditional marketing authorization as it is reserved to medicinal products to be approved for severe diseases or unmet medical needs and the applicant does not hold the complete data set legally required for the grant of marketing authorization. However, unlike the conditional marketing authorization, the applicant does not have to provide the missing data and will never have to. Although marketing authorization "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the marketing authorization is withdrawn in case the risk-benefit ratio is no longer favorable. Under these procedures, before granting the marketing authorization, EMA or the competent authorities of the member states make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety, and efficacy. Except conditional marketing authorizations, marketing authorizations have an initial duration of five years. After these five years, the authorization may be renewed on the basis of a reevaluation of the risk-benefit balance.

Pediatric Studies in the EU

Prior to obtaining a marketing authorization in the European Union, sponsors 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 United States, 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, orSmPC, 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 sponsor 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 sponsor can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (2) the sponsor consents to a second orphan medicinal product application; or (3) the sponsor cannot supply enough orphan medicinal product.

Pediatric Exclusivity in the EU

If a sponsor 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

The UK's withdrawal from the EU, commonly referred to as Brexit, took place on January 31, 2020. The EU and the UK reached an agreement on their new partnership in the Trade and Cooperation Agreement, which entered into force on May 1, 2021. As of January 1, 2021, the Medicines and Healthcare Products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland continues to be subject to EU rules under the Northern Ireland Protocol, as amended by the so called Windsor Framework agreed in February 2023. As of January 1, 2025, the changes introduced by the Windsor Framework resulted in the MHRA being responsible for approving all medicinal products destined for the United Kingdom market (Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. The MHRA relies on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR as the basis for regulating medicines. The HMR has incorporated into the domestic law the body of EU law instruments governing medicinal products that pre-existed prior to the UK's withdrawal from the EU.

As of January 1, 2024 on, a new international recognition procedure, or IRP applies which intends to facilitate approval of pharmaceutical products in the UK. The IRP is open to applicants that have already received an authorization for the same product from one of the MHRA's specified Reference Regulators, or RRs. The RRs notably include EMA and regulators in the EEA member states for approvals in the EU centralized procedure and mutual recognition procedure as well as the FDA (for product approvals granted in the U.S.). The RR assessment must have undergone a full and standalone review. RR assessments based on reliance or recognition cannot be used to support an IRP application. A CHMP positive opinion or a Mutual Recognition/Decentralized Reliance Procedure positive end of procedure outcome is an RR authorization for the purposes of IRP.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EEA, including personal health data, is subject to the GDPR, which became effective on May 25, 2018. In the United Kingdom, the GDPR is retained in domestic law as the UK GDPR and sits alongside an amended version of the UK Data Protection Act 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States, 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 of the respective group of companies, 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 October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-U.S. Privacy Shield. The European Union initiated the process to adopt an adequacy decision for the EU-U.S. Data Privacy Framework in December 2022 and the European Commission adopted the adequacy decision on July 10, 2023. The adequacy decision will permit U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the European Union to the United States. However, some privacy advocacy groups have already suggested that they will be challenging the EU-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms.

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;
- 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 HHS, information related to payments and other transfers of value to certain healthcare providers 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 and Pharmaceutical Pricing

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.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. 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 pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid.

On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year. On August 15, 2024, HHS published the results of the first Medicare drug price negotiations for ten selected drugs. On January 17, 2025, CMS announced its selection of 15 additional drugs covered by Part D for the second cycle of negotiations.

On June 6, 2023, Merck & Co. filed a lawsuit against HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, other parties also filed lawsuits in various courts with similar constitutional claims against HHS and CMS. HHS has generally won the substantive disputes in these cases. Certain of these cases are now on appeal. Litigation involving these and other provisions of the IRA will continue with unpredictable and uncertain results.

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. This is increasingly true with respect to products approved pursuant to the accelerated approval pathway. State Medicaid programs and other payers are developing strategies and implementing significant coverage barriers, or refusing to cover these products outright, arguing that accelerated approval drugs have insufficient or limited evidence despite meeting the FDA's standards for accelerated approval. 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 Resources

As December 31, 2024, we had 705 full-time employees and five part-time employees. Of these employees, 603 were based in the United States, 107 were based in international locations and 93 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 recognize that there is still important progress to be made, and this remains an area of continued emphasis for us.

We care for the health, well-being, and futures of our employees and their families. To incentivize and reward strong performance, we have competitive compensation and benefits programs, including short-term and long-term incentives, health and wellness benefits along with vacation and leave programs. We offer an array of flexible working options that balances the needs of our employees with business needs.

We offer equity incentives to all new employees and an annual equity award to all our employees in connection with our annual performance reviews and regular Total Rewards programs. Our equity and cash incentive plans are aimed to increase stockholder value and the success of our company by motivating our employees to perform to the best of their abilities and achieve our and their objectives. In addition, many of our employees are stockholders of our company through participation in our Employee Stock Purchase Plan, which aligns the interests of our employees with our stockholders by providing stock ownership on a tax-deferred basis. We also provide up to a 50% match on employee contributions (up to 5% of base salary) to our 401(k) retirement savings plan.

Our full-time U.S. employees are all eligible to participate in our health, vision, dental, life, and long-term disability insurance plans. To encourage employees to keep up with routine medical care and participate in our wellness program, we fund a health reimbursement account for participating employees and to help our employees cover medical expenses pre-tax, we also offer employees a flexible spending account. Our employees outside of the United States receive competitive compensation and benefits that are regularly benchmarked to ensure market norms and reflect our standards. All employees globally have access to complimentary virtual fitness programs, mental and emotional health support services, as well as support programs to assist working parents with childcare and tutoring. This benefit also extends to eldercare, pet care, and other needs facing our diverse global team.

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.

Corporate Responsibility

We are highly committed to policies and practices focused on sustainability, positively impacting our community and maintaining and cultivating good corporate governance. By focusing on such policies and practices, we strive to bring transformative medicines to patients, provide an engaging and inclusive workplace for our employees, minimize our impact on the environment, and always demonstrate integrity in our actions.

Information in any ESG Sustainability Report that we may publish is not incorporated by reference into this Form 10-K. We look forward to continuing our commitment to giving back to our local communities in 2025 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, or the SEC, 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 Securities and Exchange Commission, or 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 expenses, and may never achieve or maintain profitability.

We have incurred significant annual net operating losses in every year since our inception. We expect to continue to incur significant expenses for the foreseeable future. Our net losses were $197.9 million, $528.6 million and $652.2 million for the years ended December 31, 2024, 2023 and 2022 respectively. As of December 31, 2024, we had an accumulated deficit of $3.0 billion. While we are now generating substantial revenue from sales of SYFOVRE and EMPAVELI, we have primarily financed our operations to date through the sale of our common stock in our public 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 financing agreement with Sixth Street Lending Partners, or Sixth Street, and the collaboration agreement with Swedish Orphan Biovitrum AB (Publ), or Sobi. 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 the commercialization of SYFOVRE and EMPAVELI. Our operating results 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 for the foreseeable future and may incur operating losses for at least this year. We anticipate that we will continue to incur increasing expenses if and as we:

- continue to commercialize EMPAVELI in the United States and commercialize SYFOVRE for the treatment of GA in the United States, Australia, and select other jurisdictions;
- prioritize the ongoing development of systemic pegcetacoplan and focus our research initiatives on high potential opportunities;
- establish and continue to build sales, marketing, distribution and other commercial infrastructure for EMPAVELI and SYFOVRE and any other products for which we may obtain marketing approval;
- prepare to submit additional applications for regulatory approval for SYFOVRE outside the United States;
- continue to develop and conduct research and preclinical and clinical trials of our current and future product candidates;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical trials, if any;
- continue to manufacture commercial quantities of our approved products and to manufacture our product candidates for clinical development and, potentially, commercialization;
- maintain, expand and protect our intellectual property portfolio;
- hire and retain personnel;
- add operational, financial and management information systems; 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 product revenue. Our ability to generate significant revenue will require us to successfully commercialize EMPAVELI and SYFOVRE in the approved indications. While we have generated product revenue from sales of EMPAVELI since May 2021 and SYFOVRE in March 2023, we have not generated sufficient revenue to achieve profitability and there can be no assurance that we will generate sufficient revenue to achieve

profitability in the next several years, or at all. Even if we achieve profitability, there can be no assurance that we will be able to maintain profitability.

The successful commercialization of our approved products 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 will be sufficient for us to become profitable for several years, if at all. Our prospects depend substantially upon the commercial success of SYFOVRE.

Successful commercialization will require manufacturing, marketing and selling our approved products, 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 are continuing to devote significant resources to support our ongoing commercial activities related to product manufacturing, marketing, sales and distribution of EMPAVELI for PNH and SYFOVRE for GA, and if our cash, cash equivalents, and cash generated from sales of EMPAVELI and SYFOVRE are not sufficient to fund our planned expenditures, we will need to finance our cash needs through external sources of funds.

Developing and commercializing pharmaceutical products, including conducting preclinical studies and clinical trials and preparing for commercial launch, 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, 2024, 2023 and 2022, we used net cash of $87.9 million, $594.7 million and $513.7 million respectively, in our operating activities substantially all of which related to research, development and commercialization activities. As of December 31, 2024, our cash and cash equivalents were $411.3 million. We expect our expenses to continue, particularly as we continue to commercialize EMPAVELI and SYFOVRE, and prioritize the ongoing development of pegcetacoplan and focus our research initiatives on high potential opportunities. In addition, as we continue to commercialize EMPAVELI and SYFOVRE, and if we obtain marketing approval of pegcetacoplan in other indications or jurisdictions or for our other product candidates, we expect we will incur significant additional commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of a collaborator.

We believe that our cash and cash equivalents as of December 31, 2024, together with the cash that we anticipate will be generated from sales of EMPAVELI and SYFOVRE will be sufficient to fund our projected operating expenses and capital expenditure requirements for at least the next 12 months, as well as our anticipated longer-term cash requirements and obligations. Our expectations regarding our short-term and long-term funding requirements are based on assumptions that may prove to be wrong, and we may need additional capital resources to fund our operating plans and capital expenditure requirements.

We are devoting substantial resources to the commercialization of SYFOVRE for GA. We are also devoting substantial resources to the preparation for commercialization of EMPAVELI for the treatment of C3G and IC-MPGN, our planned Phase 3 clinical trials of EMPAVELI for the treatment of FSGS and DGF, and the development of our product candidates. Because of the numerous risks and uncertainties associated with the commercialization of EMPAVELI and SYFOVRE and development of other product candidates, and because the extent to which we may enter into collaborations with third parties for any of these activities is unknown, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with the research, development and commercialization. Our future funding requirements and long-term capital requirements will depend on many factors, including:

- our ability to successfully commercialize and sell EMPAVELI in the United States and SYFOVRE in the United States, Australia and select other jurisdictions;
- the cost of and our ability to obtain regulatory approvals of SYFOVRE outside of the United States;
- the cost of and our ability to effectively establish and maintain, the commercial infrastructure and manufacturing capabilities required to support the commercialization of EMPAVELI for PNH, systemic pegcetacoplan and SYFOVRE 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, SYFOVRE 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 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 public health crises, including pandemics and epidemics, 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 and SYFOVRE or any other product we commercialize;

If our cash and cash equivalents, and the cash generated from sales of EMPAVELI and SYFOVRE are not sufficient to fund our planned expenditures, we will need to finance our cash needs through external sources of funds, which may include equity offerings, debt financings, collaborations, strategic alliances or licensing arrangements. We currently do not have any committed external sources of funds.

If we are unable to generate sufficient funds from sales of EMPAVELI and SYFOVRE or 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.

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 to continue to incur significant expenses 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.

Future debt securities or other financing arrangements could contain similar or more restrictive negative covenants. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

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

The terms of our indebtedness could adversely affect our operations and limit our ability to plan for or respond to changes in our business. If we are unable to comply with restrictions in our debt financing agreements, the repayment of our existing indebtedness could be accelerated.

As of December 31, 2024, we had $375 million of indebtedness under our financing agreement with Sixth Street and approximately $93.9 million principal amount of the Convertible Notes outstanding and held by third parties as of December 31, 2024. We may also incur additional indebtedness to meet future financing needs.

Under our financing agreement, or the Sixth Street Financing Agreement, by and among us, certain of our subsidiaries, the lenders party thereto and Sixth Street, as the administrative agent for the lenders, we have incurred a substantial amount of debt, which could adversely affect our business. In May 2024, we drew down the senior secured term loan facility, or the Credit Facility, of $375.0 million. The Credit Facility also includes a potential additional $100.0 million draw at our option upon satisfaction of a $50.0 million minimum cash requirement and a requirement that our trailing three-month sales of SYFOVRE were at least $180.0 million prior to the $100.0 million draw. Among other permissions, we are permitted, on terms and conditions set forth on the Sixth Street Financing Agreement, to enter into a separate asset-based financing arrangement with a third party in an amount of up to $100.0 million, which amount is increased to $200.0 million upon certain sales or market capitalization thresholds, and to have outstanding convertible unsecured notes in an amount equal to the greater of $400.0 million and 10% of our market capitalization, but not to exceed $600.0 million.

The Sixth Street Financing Agreement requires us to make certain payments of interest over time and contains several other negative covenants that, subject to certain exceptions, restrict indebtedness, liens, investments (including acquisitions), fundamental changes, asset sales and licensing transactions, dividends, modifications to material agreements, payment of subordinated indebtedness, and other matters customarily restricted in such agreements. Among other requirements of the Sixth Street Financing Agreement, we and our subsidiaries party to the Sixth Street Financing Agreement must maintain liquidity of at least $50.0 million if our market capitalization is below $3.0 billion. We are also subject to restrictions on sales and licensing transactions with respect to our core intellectual property, defined to include SYFOVRE, EMPAVELI, and other pegcetacoplan product assets, subject to certain exceptions, including certain transactions related to areas outside the United States and Europe. These and other terms in the Sixth Street Financing Agreement could restrict our ability to grow our business or enter into transactions that we believe would be beneficial to our business.

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.

Furthermore, 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.

Our indebtedness could affect our business in the following ways, among other things: make it more difficult for us to satisfy our contractual and commercial commitments; require us to use a substantial portion of our cash flow from operations to pay interest and principal when due, which would reduce funds available for working capital, capital expenditures and other general corporate purposes; limit our ability to obtain additional financing for working capital, capital expenditures, acquisitions and other investments or general corporate purposes; heighten our vulnerability to downturns in our business, our industry or in the general economy; place us at a disadvantage compared to those of our competitors that may have proportionately less debt; limit management's discretion in operating our business; and limit our flexibility in planning for, or reacting to, changes in our business, the industry in which we operate or the general economy.

Our business may not generate cash flows from operations in the future that are sufficient to service our debt and support our growth strategies. If we are unable to generate such cash flows, we may be required to adopt one or more alternatives, such as obtaining additional equity capital on terms that may be onerous or highly dilutive, selling assets, or restructuring debt. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at such time. 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 have substantial accounts receivable, and any delays in collecting accounts receivable or the failure to collect accounts receivable could have a material adverse effect on our cash flows and results of operations.

Our accounts receivable balance was $264.9 million as of December 31, 2024, which primarily consisted of EMPAVELI and SYFOVRE product sales receivable(s) and licensing and other revenue receivables from our collaboration with Sobi. While we monitor the financial performance and creditworthiness of our customers and provide reserves against trade receivables for expected credit losses that may result from a customer's failure to pay, no assurances can be made that we will not experience delays in collecting payments, that we will collect the payments due to us. Sales to a small number of distributors account for substantially all our gross revenue related to SYFOVRE during the year ended December 31, 2024. Distributors require industry-standard payment terms, including an extended time period for distributors to make payments to Apellis. Any failures to receive cash payments could have a material adverse effect on our results of operations and cash flows. We do not have a reserve related to expected credit losses against our accounts receivable balance.

Risks Related to the Commercialization and Product Development

Our business and prospects are substantially dependent on the success of SYFOVRE and EMPAVELI and the successful development and commercialization of pegcetacoplan in other jurisdictions and disease indications, including C3G and IC-MPGN. If we are unable to continue to successfully commercialize SYFOVRE and EMPAVELI, or develop, obtain marketing approval for or successfully commercialize systemic pegcetacoplan in other indications and jurisdictions, 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 SYFOVRE and EMPAVELI and development of systemic pegcetacoplan in other disease indications and jurisdictions. Our prospects are substantially dependent on our ability, or that of Sobi or any future collaborator, to successfully commercialize EMPAVELI in the United States and SYFOVRE worldwide and to develop, obtain marketing approval for and successfully commercialize systemic pegcetacoplan in additional disease indications. SYFOVRE is currently only approved in the United States and Australia. We did not obtain regulatory approval in the European Union, which has adversely affected our business and prospects. We cannot be certain that we will be able to obtain regulatory approval for, and successfully commercialize, SYFOVRE in any additional jurisdiction. Our prospects are dependent on the success of pegcetacoplan, including C3G and IC-MPGN, and our ability to obtain additional marketing approvals for pegcetacoplan in these or other indications. Pursuant to our agreement with Sobi, we have granted to Sobi the exclusive right to commercialize systemic pegcetacoplan outside the United States. All of our product candidates other than pegcetacoplan are in early stages of development

The success of EMPAVELI in PNH, SYFOVRE in GA and pegcetacoplan in C3G and IC-MPGN and in other indications will depend on several factors, including the following:

- our ability to successfully commercialize and sell EMPAVELI in the United States and SYFOVRE in the United States, Australia and select other jurisdictions;
- commercial acceptance by patients, the medical community and third-party payors of EMPAVELI in PNH, SYFOVRE in GA, pegcetacoplan in C3G and IC-MPGN and in other indications, if approved, and other product candidates, if approved;
- initiation and successful recruitment of patients, enrollment in and completion of our ongoing and planned clinical trials, including our planned Phase 3 clinical trials with systemic pegcetacoplan in the second half of 2025 for the treatment of FSGS and DGF;
- 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;
- our ability to submit and obtain marketing approvals for SYFOVRE in additional jurisdictions;

- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- establishment of arrangements with third-party suppliers and manufacturers for raw materials, drug intermediates, and 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;
- 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 the results of clinical development, the regulatory approval 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, C3G and IC-MPGN, SYFOVRE in the United States and select other jurisdictions for GA, or to develop, receive marketing approval for and successfully commercialize pegcetacoplan in other indications or jurisdictions 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.

We or others may later discover that EMPAVELI or SYFOVRE is less effective than previously believed or causes safety issues that were not identified in clinical trials, 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 safety issues that may be observed once the product has been commercialized. If safety problems occur or are identified with EMPAVELI or SYFOVRE or with any other product of ours that reaches the market, if any, 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.

A small number of patients treated with SYFOVRE in the real world have experienced retinal vasculitis, a severe form of intraocular inflammation. We plan to continue to submit all adverse events reported to us to the FDA consistent with reporting guidelines for drug manufacturers.

We cannot provide any assurances and the retinal community will believe that the expected benefits of SYFOVRE treatment outweigh its potential risks to patients in light of these reported events or other events that might arise or that our applications for marketing approval of SYFOVRE in other jurisdictions will not be adversely impacted by these events. A change in the perception of the benefit/risk profile of SYFOVRE may reduce market acceptance of the product and our product revenues may be adversely affected.

If we, or others, discover that a product is less effective than previously believed or causes safety issues that were not previously identified, such as the reported events of retinal vasculitis following SYFOVRE treatment, any of the following events could occur:

- the target patient population may be less willing to try, and physicians may be less willing to prescribe, the product;
- 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, affect sales of our products and 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 EMPAVELI or SYFOVRE, in which case we may not generate significant revenues or become profitable, and the market opportunity for these products may be smaller than we estimate.

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 EMPAVELI or SYFOVRE.

Our commercial strategy for EMPAVELI for PNH is to maintain patients currently on treatment and drive growth by reinforcing EMPAVELI's differentiated efficacy profile, long-term data and real-world experience. 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, they are required to switch therapies due to lack of reimbursement for existing therapies, or they are not responding well to their existing therapy. If patients decide to switch their therapy, many may prefer an orally administered therapy, such as iptacopan, for convenience reasons.

There are no current treatment options approved for C3G and IC-MPGN. We anticipate that a competitive product, iptacopan, may be approved and marketed prior to EMPAVELI. Our commercial strategy for EMPAVELI for C3G and IC-MPGN is to raise awareness on disease diagnosis, understand the important role of C3 as a driver of disease, recognize the limitations of symptom management, and drive understanding of EMPAVELI's differentiated efficacy profile. If physicians and patients choose to initiate therapy, EMPAVELI is a self-administered subcutaneous injection and may not be the preferred route of administration.

Our commercial strategy for SYFOVRE is to educate the ophthalmology and retina communities on the urgency to diagnose and treat GA, and to establish SYFOVRE as the preferred product due to its differentiated efficacy, flexible dosing options, and real-world utilization. The commercial efforts are also aimed at increasing the breadth of SYFOVRE utilization and experience among treating retina physicians and ensuring broad and sustained access with payors.

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, SYFOVRE, or any of our product candidates for which we obtain marketing approval do not achieve an adequate level of market acceptance, we may not generate significant revenues and we may not become profitable. The degree of market acceptance of EMPAVELI, SYFOVRE, 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, SYFOVRE in GA, or in any other indication is difficult to precisely estimate. Our estimates of the potential market opportunity for EMPAVELI in PNH, C3G and IC-MPGN, FSGS and DGF, and SYFOVRE in GA, or in other indications include several key assumptions based on our industry knowledge, industry publications, scientific literature, 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 and C3G and IC-MPGN, SYFOVRE in GA, or any other future indication could be smaller than our estimates of potential market opportunity. If the actual market for EMPAVELI in PNH, SYFOVRE in GA, in other future 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 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 each of EMPAVELI and SYFOVRE. 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, SYFOVRE, or any product candidates that we are currently developing or that we may develop, which could render EMPAVELI, SYFOVRE, 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. Furthermore, in December 2023, the FDA approved iptacopan (marketed as Fabhalta), an orally administered factor B inhibitor developed by Novartis, for the treatment of PNH. This product may have a competitive advantage if prescribers and patients prefer to utilize an oral medication rather than an injected medication. 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 systemic programs. In 2022, AstraZeneca also obtained approval for a subcutaneous version of ravulizumab, currently in phase 3 clinical trial.

SYFOVRE was the first approved product in the United States for the treatment of GA. In August 2023, the FDA approved avacincaptad pegol, marketed as Izervay, a complement C5 inhibitor developed by Astellas Pharma Inc., 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 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 approval for SYFOVRE for the treatment of patients with GA in the United States and Australia, but there is no assurance that we will receive regulatory approvals for SYFOVRE for the treatment of GA in other jurisdictions. For example, in 2024, the European Commission adopted a negative opinion on the MAA for SYFOVRE in the European Union, despite positive recommendations from the ad hoc expert groups convened by the EMA and a significant number of dissenting votes from European Union member states. Because regulators in other jurisdictions are influenced by decisions of the FDA and the EMA, negative opinion by the FDA or the EMA may adversely impact the prospects for approval in other jurisdictions. We have received approval for EMPAVELI for the treatment of patients with PNH in several jurisdictions, but there is no assurance that we will receive regulatory approvals for EMPAVELI in other indications, including C3G and IC-MPGN.

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.

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 clinical 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.

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.

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.

For example, in January 2024, we and Sobi agreed to cease clinical development of systemic pegcetacoplan for patients with cold agglutinin disease, or CAD, due to the decreased medical need in CAD and the limited number of patients eligible for the CASCADE trial.

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.

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 and preliminary or interim results of clinical trials do not necessarily predict final results.

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, including APL-3007, which is a siRNA, and our FcRn gene editing treatment that we are developing through our collaboration with Beam. These product candidates utilize different mechanisms of action than EMPAVELI and SYFOVRE and we do not have experience conducting clinical trials of product candidates with such mechanisms of action. 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.

If the commercial launch of EMPAVELI and SYFOVRE, for each of 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 and SYFOVRE, 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 or SYFOVRE 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 or SYFOVRE 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 or SYFOVRE 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 or SYFOVRE, impact our ability to generate revenue and harm our business.

If we are unable to maintain our sales, marketing and distribution arrangements with third parties, we may not be successful in commercializing EMPAVELI and SYFOVRE. Similarly, 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, SYFOVRE, pegcetacoplan in other indications or any of our other product candidates for which we obtain marketing approval.

We have built a sales, marketing and distribution infrastructure in the United States to support commercialization of EMPAVELI and SYFOVRE.

We are building focused capabilities to commercialize SYFOVRE in GA and EMPAVELI in PNH, C3G and IC-MPGN 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, SYFOVRE, 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.

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 abbreviated new drug application, or 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. Pegcetacoplan received its first approval from the FDA in May 2021. 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, SYFOVRE, 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, SYFOVRE, or any of 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, SYFOVRE, 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. The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. 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. 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 or product candidate to other available therapies. Adverse pricing limitations may hinder our ability or the ability of our collaborators to recoup our or their investment in one or more products or 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, SYFOVRE, 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, SYFOVRE, 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, SYFOVRE, and coverage may be more limited for EMPAVELI and SYFOVRE 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, SYFOVRE, 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 SYFOVRE, 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, SYFOVRE, 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, SYFOVRE, or any other products that we may develop.

Although we maintain product liability and clinical trial insurance coverage in the amount of up to $50.0 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 may need to increase our insurance coverage as we continue to commercialize EMPAVELI, SYFOVRE, and commercialize 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, SYFOVRE, and our other product candidates, which could harm our business, financial condition, results of operations and prospects.

Our internal information technology 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, compromise sensitive information related to our business or prevent us from accessing critical information, trigger contractual and legal obligations, potentially exposing us to liability, reputational harm or otherwise adversely affecting our business and financial results.

We are dependent upon information technology systems, infrastructure and data to operate our business. In the ordinary course of business, 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. It is critical that we, our vendors, collaborators or other contractors or consultants, do so in a secure manner to maintain the availability, security, confidentiality, privacy and integrity of such confidential information.

Despite the implementation of security measures, our internal information technology systems and those of third parties are vulnerable to damage from computer viruses, malware, computer hackers, malicious code, employee error, theft or misuse, denial-of-service attacks, sophisticated nation-state supported actors, 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, unauthorized access to or deletion of files, 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. We may not be able to anticipate all types of security threats, and we may not be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched, and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist organizations or hostile foreign governments or agencies. We cannot guarantee that the measures we have taken to date, and actions we may take in the future, will be sufficient to prevent any future breaches.

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 or confidential 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 or our vendors', collaborators' or other contractors' or consultants' data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, including litigation exposure, penalties and fines, we could become the subject of regulatory action or investigation, 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. As a result of such an event, we may be in breach of our contractual obligations. Furthermore, any such event that leads to unauthorized access, use, or disclosure of personal information, including personal information regarding our customers or employees, could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information, which could result in significant legal and financial exposure and reputational damages. Any of the above could have a material adverse effect on our business, financial condition, results of operations or prospects.

The financial exposure from the events referenced above could either not be insured against or not be fully covered through any insurance that we maintain and could have a material adverse effect on our business, financial condition, results of operations or prospects. In addition, we cannot be sure that our existing insurance coverage will continue to be available on acceptable terms or that our insurers will not deny coverage as to any future claim. There can be no assurance that the limitations of liability in our contracts would be enforceable or adequate or would otherwise protect us from liabilities or damages as a result of the events referenced above.

Risks Related to Our Dependence on Third Parties

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

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

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

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

We contract with third parties for the manufacture, storage and distribution of commercial supply for EMPAVELI, SYFOVRE, 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, SYFOVRE, 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, SYFOVRE, 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 commercial supply of EMPAVELI and SYFOVRE and for our clinical supply of our product candidates. In particular, we have entered into commercial supply agreements with Bachem Americas, Inc., or Bachem, and NOF Corporation, or NOF, to purchase a significant portion of our requirements for the pegcetacoplan drug substance and drug intermediaries, respectively. We have also entered into long-term commercial supply agreements with other suppliers of raw materials, drug intermediaries, drug substance and drug product. We also have a separate supply agreement for the manufacture of the drug product for each of EMPAVELI and SYFOVRE. 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. If we experience other issues or delays in the future, our commercial success may be materially and adversely impacted and 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, result in lost sales of EMPAVELI and/or SYFOVRE or delay our clinical trials. 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. 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, SYFOVRE, 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 have developed the EMPAVELI injector, a custom, on-body drug delivery system that would enable patients to self-administer pegcetacoplan through subcutaneous infusion. If the EMPAVELI injector becomes unavailable, patients may need to rely upon 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.

We are developing a single dose, sterilized prefilled syringe for SYFOVRE that will provide physicians with a new way to administer SYFOVRE that requires fewer steps compared to the current administration. If the pre-filled syringe cannot be manufactured in accordance with applicable regulatory requirements or the availability of pre-filled syringe is delayed, physicians may need to rely upon the existing administration method.

Our prospects for the development and commercialization of our product candidates will depend in 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 products or 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 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.

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, or Penn, under which we license patent rights relating to a family of compounds for use in all fields. The licensed patent rights include issued U.S. and foreign patents with claims that recite a class of compounds generically covering pegcetacoplan 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 U.S. 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 requested a waiver of the U.S. manufacturing requirement in early 2021, 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 U.S. 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 U.S. 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 for the treatment of PNH in May 2021 and the EMA approved ASPAVELI for the treatment of PNH in December 2021. EMPAVELI has also been approved in the United Kingdom, Canada, Japan, Saudi Arabia and Australia. The FDA approved SYFOVRE for the treatment of GA in February 2023 and the Therapeutic Goods Administration of Australia approved SYFOVRE for the treatment of GA in January 2025. We submitted an sNDA for EMPAVELI for the treatment of C3G and IC-MPGN in the first quarter of 2025.

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. For example, in December 2022, with the passage of Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. In June 2024, as mandated by FDORA, the FDA issued draft guidance outlining the general requirements for DAPs. Unlike most guidance documents issued by the FDA, the DAP guidance when finalized will have the force of law because FDORA specifically dictates that the form and manner for submission of DAPs are specified in FDA guidance. On January 27, 2025, in response to an Executive Order issued by President Trump on January 21, 2025, on Diversity, Equity and Inclusion programs, the FDA removed this draft guidance from its website. The implications of this action are not yet known.

Further, in January 2022, the new Clinical Trials Regulation (EU) No 536/2014 became effective in the European Union and replaced the prior Clinical Trials Directive 2001/20/EC. This regulation aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the European Union. Under the coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one European Union Member State will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a clinical trials portal overseen by the EMA and available to clinical trial sponsors, competent authorities of the European Union Member States and the public.

In addition, under the Pediatric Research Equity Act, or PREA, an NDA, biologics license application, or BLA, or supplement to an NDA or BLA for certain drugs and biological products must contain data to assess the safety and effectiveness of the drug or biological product in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless the sponsor receives a deferral or waiver from the FDA. 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. The applicable legislation in the European Union also requires sponsors to either conduct clinical trials in a pediatric population in accordance with a Pediatric Investigation Plan approved by the Pediatric Committee of EMA, or to obtain a waiver or deferral from the conduct of these studies by this Committee. For any of our product candidates for which we are seeking regulatory approval in the United States or the European Union, we cannot guarantee that we will be able to obtain a waiver or alternatively complete any required studies and other requirements in a timely manner, or at all, which could result in associated reputational harm and subject us to enforcement action.

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.

Moreover, principal investigators for our future clinical trials may serve as scientific advisors or consultants to us and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or a comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore 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 or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

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, SYFOVRE, 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.

For example, in December 2024, the European Commission rejected the marketing authorization application, or MAA, for SYFOVRE in the European Union, after a negative recommendation of the Committee for Medicinal Products for Human Use, or CHMP. Because regulators in other jurisdictions are influenced by decisions of the FDA and the EMA, a negative opinion by the FDA or the EMA may adversely impact the prospects for approval in other jurisdictions.

Additionally, we could face heightened risks with respect to obtaining marketing authorization in the United Kingdom as a result of the withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. The United Kingdom is no longer part of the European Single Market and EU Customs Union. As of January 1, 2025, the Medicines and Healthcare products Regulatory Agency, or MHRA, is responsible for approving all medicinal products destined for the UK market (i.e., Great Britain and Northern Ireland). At the same time, a new international recognition procedure, or IRP, will apply, which intends to facilitate approval of pharmaceutical products in the United Kingdom. The IRP is open to applicants that have already received an authorization for the same product from one of the MHRA's specified Reference Regulators, or RRs. The RRs notably include EMA and regulators in the European Union/European Economic Area, or EEA, member states for approvals in the European Union centralized procedure and mutual recognition procedure as well as the FDA (for product approvals granted in the U.S.). However, the concrete functioning of the IRP is currently unclear. Any delay in obtaining, or an inability to obtain, any marketing approvals may force us or our collaborators to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business.

In addition, foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products (potentially reducing the duration of regulatory data protection, revising the eligibility for expedited pathways, etc.) was published on April 26, 2023. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may however have a significant impact on the pharmaceutical industry and our business in the long term.

We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the United States, including tariffs, trade barriers and regulatory requirements; economic weakness, including inflation, or political instability in particular foreign economies and markets; compliance with tax, employment, immigration and labor laws for employees living or traveling outside of the United States; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States.

We intend to conduct certain of our clinical trials globally . However, the FDA and other foreign equivalents may not accept data from such trials, in which case our development plans will be delayed, which could materially harm our business.

We have conducted and intend to continue conducting certain of our clinical trials globally. The acceptance by the FDA or other regulatory authorities of study data from clinical trials conducted outside their jurisdiction may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to good clinical practices, or GCP, regulations; and (iii) the data may be considered valid without the need

for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and which may result in current or future product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.

Conducting clinical trials outside the United States also exposes us to additional risks, including risks associated with:

- additional foreign regulatory requirements;
- foreign exchange fluctuations;
- compliance with foreign manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research;
- diminished protection of intellectual property in some countries; and
- interruptions or delays in our trials resulting from geopolitical events, such as war or terrorism.

We may seek certain designations for our product candidates, including Breakthrough Therapy, Fast Track and Priority Review in the United States, and PRIME (priority medicines) in the European Union, but we might not receive such designations, and even if we do, such designations may not lead to a faster development or regulatory review or approval process.

We may seek certain designations for one or more of our product candidates that could expedite review and approval by the FDA. A Breakthrough Therapy product is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious 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. For products that have been designated as Breakthrough Therapies, early and frequent interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development.

The FDA may also 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 NDA before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of data submitted by the sponsor, that a Fast Track product may be effective.

We may also seek a priority review designation for one or more of our product candidates. If the FDA determines that a product candidate intended to treat a serious condition and, if approved, offers a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation shortens the goal for the FDA to review an application within six months, rather than the standard review period of ten months.

These designations require a sponsor to submit an application for review and approval by the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for these designations, the FDA may disagree and instead determine not to make such designation. Further, even if we receive a designation, the receipt of such designation for a product candidate may not result in a faster development or regulatory review or approval process compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualifies for these designations, the FDA may later decide that the product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Where appropriate, we plan to pursue approval from the FDA, EMA or comparable foreign regulatory authorities through the use of accelerated registration pathways. If we are unable to obtain such approval, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, EMA or comparable regulatory

authorities, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA, EMA or such other regulatory authorities may seek to withdraw accelerated approval.

Where appropriate, we plan to pursue accelerated development strategies in areas of medical need. We may seek an accelerated approval pathway for one or more of our product candidates from the FDA, EMA or comparable foreign regulatory authorities. Under the accelerated approval provisions in the Federal Food, Drug, and Cosmetic Act, and the FDA's implementing regulations, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. 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. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. If such post-approval studies fail to confirm the drug's clinical benefit, the FDA may withdraw its approval of the drug.

In addition, there can be no assurance that we will satisfy all FDA requirements, including new provisions, that govern accelerated approval. For example, with passage of FDORA in December 2022, Congress modified certain provisions governing accelerated approval of drug and biologic products. Specifically, the new legislation authorized the FDA to require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded and to submit progress reports on its post-approval studies to the FDA every six months until the study is completed. Moreover, FDORA established expedited procedures authorizing FDA to withdraw an accelerated approval if certain conditions are met, including where a required confirmatory study fails to verify and describe the predicted clinical benefit or where evidence demonstrates the product is not shown to be safe or effective under the conditions of use. The FDA may also use such procedures to withdraw an accelerated approval if a sponsor fails to conduct any required post-approval study of the product with due diligence, including with respect to "conditions specified by the Secretary." The new procedures include the provision of due notice and an explanation for a proposed withdrawal, and opportunities for a meeting with the Commissioner or the Commissioner's designee and a written appeal, among other things. We will need to fully comply with these and other requirements in connection with the development and approval of any product candidate that qualifies for accelerated approval.

More recently, in March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. The FDA indicated that the accelerated approval pathway is commonly used for approval of oncology drugs due to the serious and life-threatening nature of cancer. Although single-arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust efficacy and safety assessment and allows for direct comparisons to an available therapy. To that end, the FDA outlined considerations for designing, conducting, and analyzing data for trials intended to support accelerated approvals of oncology therapeutics. Subsequently, in December 2024 and January 2025, the FDA issued additional draft guidances relating to accelerated approval. These guidances describe FDA's views on what it means to conduct a confirmatory trial with due diligence and how the agency plans to interpret whether such a study needs to be underway at the time of approval. While these guidances are currently only in draft form and will ultimately not be legally binding even when finalized, we will need to consider the FDA's guidances if we seek accelerated approval for any of our products in the future.

Prior to seeking accelerated approval, we will seek feedback from the FDA, EMA or comparable foreign regulatory authorities and will otherwise evaluate our ability to seek and receive such accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that after subsequent feedback from the FDA, EMA or comparable foreign regulatory authorities, we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or under another expedited regulatory designation (i.e., Fast Track designation, Breakthrough Therapy designation or orphan drug designation), there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA, EMA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidate would result in a longer time period to commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

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 and C3G, 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 and Congress may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the Court of Appeals for the 11th Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term "same disease or condition" means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Thus, the court concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the "indication or use." Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, the FDA announced that, in matters beyond the scope of that court order, the FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved. 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.

The FDA, EMA and other regulatory authorities actively enforce the laws and regulations prohibiting the promotion of off-label uses.

If any of our product candidates are approved and we are found to have improperly promoted off-label uses of those products, we may become subject to significant liability. The FDA, EMA and other regulatory authorities strictly regulate the promotional claims that may be made about prescription products, such as our product candidates, if approved. In particular, a product may not be promoted in the United States for uses that are not approved by the FDA as reflected in the product's approved labelling, or in other jurisdictions for uses that differ from the labelling or uses approved by the applicable regulatory authorities. While physicians may prescribe products for off-label uses, the FDA, EMA and other regulatory authorities actively enforce laws and regulations that prohibit the promotion of off-label uses by companies, including promotional communications made by companies' sales force with respect to off-label uses that are not consistent with the approved labelling, and a company that is found to have improperly promoted off-label uses may be subject to significant civil, criminal and administrative penalties.

Notwithstanding the regulatory restrictions on off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional scientific communications concerning their products in certain circumstances. For example, in October 2023, the FDA published draft guidance outlining the agency's non-binding policies governing the distribution of scientific information on unapproved uses to healthcare providers. This draft guidance calls for such communications to be truthful, non-misleading, factual, and unbiased and include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use. In addition, under some relatively recent guidance from the FDA and the Pre-Approval Information Exchange Act, or PIE Act, signed into law as part of the Consolidated Appropriations Act of 2023, companies may also promote information that is consistent with the prescribing information and proactively speak to formulary committee members of payors regarding data for an unapproved drug or unapproved uses of an approved drug. We may engage in these discussions and communicate with healthcare providers, payors and other constituencies in compliance with all applicable laws, regulatory guidance and industry best practices. We will need to carefully navigate the FDA's

various regulations, guidance and policies, along with recently enacted legislation, to ensure compliance with restrictions governing promotion of our products.

We will also need to observe the FDA's various regulations, guidance and policies, along with recently enacted legislation, to ensure compliance with restrictions governing promotion of our products. In September 2021, the FDA published final regulations which describe the types of evidence that the Agency will consider in determining the intended use of a drug or biologic. In addition, in January 2025, the FDA published final guidance outlining its policies governing the distribution of scientific information to healthcare providers about unapproved uses of approved products. The final guidance calls for such communications to be truthful, non-misleading and scientifically sound and to include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use of the approved product. If a company engages in such communications consistent with the guidance's recommendations, the FDA indicated that it will not treat such communications as evidence of unlawful promotion of a new intended use for the approved product.

If we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

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 and SYFOVRE in accordance with their approved label in each jurisdiction and may not promote them for any indication other than as stated on the label. The label for Aspaveli in the European Union is more limited than the label for EMPAVELI in the United States.

EMPAVELI, SYFOVRE, 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, SYFOVRE, 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, SYFOVRE, 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.

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.

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.

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 for which we receive marketing approval 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.

There is substantial uncertainty as to how, if at all, the Trump administration will seek to modify or revise the requirements and policies of the FDA and other regulatory agencies with jurisdiction over our product candidates. The impending uncertainty could present new challenges or potential opportunities as we navigate the clinical development and approval process for our product candidates.

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.

In addition, disruptions may still result also from the recent COVID-19 pandemic or any similar event that may occur in the future. During the recent COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the

FDA's inability to complete required inspections for their applications. In the event of a similar public health emergency in the future, the FDA may not be able to continue its current pace and review timelines could be extended. Regulatory authorities outside the United States facing similar circumstances may adopt similar restrictions or other policy measures in response to a similar public health emergency and may also 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, SYFOVRE, 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.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid.

In August 2022, the IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least nine years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Nonetheless, since CMS may establish a maximum price for these products in price negotiations, we would be fully at risk of government action if our products are the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also further heighten the risk that we would not be able to achieve the expected return on our drug products or full value of our patents protecting our products if prices are set after such products have been on the market for nine years.

Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year. On August 15, 2024, HHS published the results of the first Medicare drug price negotiations for ten selected drugs. On January 17, 2025, CMS announced its selection of 15 additional drugs covered by Part D for the second cycle of negotiations.

On June 6, 2023, Merck & Co. filed a lawsuit against HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, other parties also filed lawsuits in various courts with similar constitutional claims against HHS and CMS. HHS has

generally won the substantive disputes in these cases. Certain of these cases are now on appeal. Litigation involving these and other provisions of the IRA will continue with unpredictable and uncertain results.

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. This is increasingly true with respect to products approved pursuant to the accelerated approval pathway. State Medicaid programs and other payers are developing strategies and implementing significant coverage barriers, or refusing to cover these products outright, arguing that accelerated approval drugs have insufficient or limited evidence despite meeting the FDA's standards for accelerated approval. 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 addition, in some countries, including member states of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take a significant amount of time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic, and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices, and in certain instances render commercialization in certain markets infeasible or disadvantageous from a financial perspective. In some countries, we or our collaborators may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product and/or our product candidates to other available products in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third party payors or government authorities may lead to further pressure on the prices or reimbursement levels. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, the commercial launch of our product and/or product candidates could be delayed, possibly for lengthy periods of time, we or our collaborators may not launch at all in a particular country, we may not be able to recoup our investment in one or more product candidates, and there could be a material adverse effect on our business.

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 certain healthcare providers and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members;

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 U.K. 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, 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) sponsor 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 sponsor 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 sponsor 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, SYFOVRE, 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.

We are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of personally-identifying information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information, including comprehensive regulatory systems in the United States, European Union and United Kingdom The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. Failure to comply with any of these laws and regulations could result in enforcement action against us, including fines, claims for damages by affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

There are numerous U.S. federal and state laws and regulations related to the privacy and security of personal information. In particular, regulations promulgated pursuant to HIPAA establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Determining whether protected health information has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation. These obligations may be applicable to some or all of our business activities now or in the future.

If we are unable to properly protect the privacy and security of protected health information, we could be found to have breached our contracts. Further, if we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties. HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

Similar to the laws in the United States, there are significant privacy and data security laws that apply in Europe and other countries. 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 regulated by the GDPR, which went into effect in May 2018 and which imposes obligations on companies that operate in our industry with respect to the processing of personal data and the cross-border transfer of such data. The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and policies. If our or our partners' or service providers' privacy or data security measures fail to comply with the GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data and/or fines of up to 20 million Euros or up to

4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, as well as compensation claims by affected individuals, negative publicity, reputational harm and a potential loss of business and goodwill.

The GDPR places restrictions on the cross-border transfer of personal data from the European Union to countries that have not been found by the EC to offer adequate data protection legislation, such as the United States. There are ongoing concerns about the ability of companies to transfer personal data from the EU to other countries. In July 2020, the Court of Justice of the European Union, or the CJEU, invalidated the EU-U.S. Privacy Shield, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the U.S. 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 U.S. While we were not self-certified under the Privacy Shield, this CJEU decision may lead to increased scrutiny on data transfers from the EEA to the U.S. generally and increase our costs of compliance with data privacy legislation as well as our costs of negotiating appropriate privacy and security agreements with our vendors and business partners.

Beyond GDPR, there are privacy and data security laws in a growing number of countries around the world. While many loosely follow GDPR as a model, other laws contain different or conflicting provisions. These laws will impact our ability to conduct our business activities, including both our clinical trials and the sale and distribution of commercial products, through increased compliance costs, costs associated with contracting and potential enforcement actions.

While we continue to address the implications of the recent changes to data privacy regulations, data privacy remains an evolving landscape at both the domestic and international level, with new regulations coming into effect and continued legal challenges, and our efforts to comply with the evolving data protection rules may be unsuccessful. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. We must devote significant resources to understanding and complying with this changing landscape. Failure to comply with laws regarding data protection would expose us to risk of enforcement actions taken by data protection authorities in the EEA and elsewhere and carries with it the potential for significant penalties if we are found to be non-compliant. Similarly, failure to comply with federal and state laws in the U.S. regarding privacy and security of personal information could expose us to penalties under such laws. Any such failure to comply with data protection and privacy laws could result in government-imposed fines or orders requiring that we change our practices, claims for damages or other liabilities, regulatory investigations and enforcement action, litigation and significant costs for remediation, any of which could adversely affect our business. 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 business, financial condition, results of operations or prospects.

A variety of risks associated with international operations could materially adversely affect our business.

As we engage in significant cross-border and international activities, we will be subject to risks related to international operations, including:

- different regulatory requirements for initiating clinical trials and maintaining approval of drugs in foreign countries;
- reduced protection for intellectual property rights in certain countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, political instability or open conflict in particular foreign economies and markets;
- differing and multiple payor reimbursement regimes, government payers or patient self-pay systems;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations of doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in North America;
- controlled substance legislation differs between countries and legislation in certain countries may restrict, limit, or delay our ability to manufacture and/or transport our product candidates;
- likelihood of potential or actual violations of domestic and international anti-corruption laws, such as the U.S. Foreign Corrupt Practices Act and the U.K. Bribery Act, or of U.S. and international import, export and re-export control and sanctions laws and regulations, which likelihood may increase with an increase of operations in foreign jurisdictions, directly or indirectly through third parties (whose corrupt or other illegal conduct may subject us to liability), which may involve interactions with government agencies or government-affiliated hospitals, universities and other organizations, such as conducting clinical trials, selling our products, and obtaining necessary permits, licenses, patent registrations, and other regulatory approvals

- tighter restrictions on privacy and data protection, and more burdensome obligations associated with the collection, use and retention of data, including clinical data and genetic material, may apply in jurisdictions outside of North America;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- business interruptions resulting from geopolitical actions, including war, terrorism, and civil and political unrest (such as the ongoing conflicts in the Middle East and between Russia and Ukraine), or natural disasters including earthquakes, typhoons, floods and fires; and
- supply and other disruptions resulting from the impact of public health epidemics, including the COVID-19 pandemic, on our strategic partners, third-party manufacturers, suppliers and other third parties upon which we rely.

Laws and regulations governing our international operations 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 Department of Justice 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 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 United States 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.

We have conducted, and continue to conduct, clinical trials in various jurisdictions, including Russia and other Eastern European countries. In response to the conflict between Russia and Ukraine, the United States, the European Union, and other jurisdictions have imposed economic sanctions and other restrictions against certain officials, individuals, entities, regions, and industries in Russia, Ukraine, and Belarus. Such sanctions, and any further restrictions that may be promulgated, could adversely impact our ability to conduct our clinical program in certain jurisdictions. We will continue to closely monitor the geopolitical situation in Ukraine and its impact on our clinical trial operations.

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.

Changes in U.S. and international trade policies may adversely impact our business and operating results.

The U.S. government has recently made statements and taken, or has contemplated taking, certain actions that may lead to potential changes to U.S. and international trade policies, including imposing tariffs and export control restrictions affecting products manufactured outside the United States. Some of our manufacturers and suppliers are located outside the United States. Any unfavorable government policies on international trade, such as export controls, capital controls or tariffs, may increase the cost of manufacturing our product candidates and platform materials, affect the demand for our drug products (if and once approved), the competitive position of our product candidates, and import or export of raw materials and finished product candidate used in our and our collaborators' preclinical studies and clinical trials, particularly with respect to any product candidates and materials that we import. If any new tariffs, export controls, legislation and/or regulations are implemented, or if existing trade agreements are renegotiated or, in particular, if either the U.S. or any foreign government takes retaliatory trade actions, such changes could have an adverse effect on our business, financial condition and results of operations.

Moreover, trade tensions and conflicts between the United States and China in particular have been escalating in recent years and, as such, we are exposed to the possibility of product supply disruption and increased costs and expenses in the event of changes to the laws, rules, regulations and policies of the governments of the U.S. or China, or due to geopolitical unrest and unstable economic conditions. Certain Chinese biotechnology companies may become subject to trade restrictions, sanctions, other regulatory requirements or proposed legislation by the U.S. government, which could restrict or even prohibit our ability to work with such entities, thereby potentially disrupting their supply of material to us. The recently proposed BIOSECURE Act introduced in the House of Representatives, as well as a substantially similar bill in the Senate, targets certain Chinese biotechnology companies. If these bills become law, or similar laws are passed, they would have the potential to severely restrict the ability of companies to contract with certain Chinese biotechnology companies of concern without losing the ability to contract with, or otherwise received funding from, the U.S. government. Such disruptions could have adverse effects on the development of our product candidates and our business 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. 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.

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. 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 commercializing EMPAVELI and SYFOVRE and obtaining regulatory approval of EMPAVELI in additional indications and jurisdictions and SYFOVRE in additional jurisdictions;
- the timing and results of clinical trials of pegcetacoplan and any other product candidates;
- the success of existing or new competitive products or technologies;
- results of discussions with regulatory authorities and regulatory actions with respect to our product candidates or our competitors' products and product candidates;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- commencement or termination of collaborations for our development programs;
- failure or discontinuation of any of our product candidates or development programs;
- results of clinical trials of product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;

- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results or development timelines;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- short positions, hedging or other transactions in our securities in connection with our Convertible Notes;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

For example, the trading price of our common stock experienced significant volatility in 2024. On January 9, 2024, the closing price of our common stock on the Nasdaq Global Select Market was $72.47 and on October 10, 2024, the closing price of our common stock on the Nasdaq Global Select Market was $27.14. Following periods of volatility in the market price of a company's stock, securities class-action litigation has often been instituted against that company. We and certain of our current and former executive officers have been named as defendants in purported class action lawsuits following our announcement of the initial, top-line results.

We and our chief executive officer have been named as defendants in lawsuits that could result in substantial costs and divert management's attention.

We, our chief executive officer, and our directors have been named as defendants in a purported class action lawsuit initiated in 2023 that alleges, among other things, that the defendants violated Sections 10(b) and/or 20(a) of the Exchange Act and Rule 10b-5 promulgated thereunder by misrepresenting and/or omitting certain material facts related to the design of SYFOVRE's clinical trials and the risks associated with SYFOVRE's commercial adoption. The plaintiffs seek, among other relief, compensatory damages and equitable relief in favor of the alleged class of plaintiffs against all defendants, including interest, and reasonable costs and expenses incurred by plaintiffs, including attorneys' and expert fees. We, our chief executive officer, and our directors have also been named as defendants in a purported stockholder derivative lawsuit initiated in 2024 that alleges, among other things that the defendants breached fiduciary duties, were unjustly enriched, committed corporate waste, and violated Section 14(a) of the Exchange Act based on the same facts. The plaintiffs seek, among other relief, monetary and punitive damages, and costs, including attorneys' fees. The outcome of the matter described above cannot be predicted with certainty. However, we intend to vigorously defend against the litigation. We are unable, however, to predict the outcome of these matters at this time. Moreover, any conclusion of these matters in a manner adverse to us and for which we incur substantial costs or damages not covered by our directors' and officers' liability insurance would have a material adverse effect on our financial condition and business. In addition, the litigation could adversely impact our reputation and divert management attention and resources from other priorities, including the execution of business plans and strategies that are important to our ability to grow our business, any of which could have a material adverse effect on our business. Additional similar lawsuits might be filed. See "Part II, Item 1-Legal Proceedings".

We have broad discretion in the use of our funds and may not use them effectively.

Our management will have broad discretion in the application of our cash and cash equivalents and could spend our funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could harm our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest our funds in a manner that does not produce income or that loses value.

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, 2023, we had options to purchase an aggregate of 8,048,307shares of our common stock outstanding, of which options to purchase 6,713,203 shares were vested and 3,061,810 outstanding unvested restricted stock units that upon vesting would result in the issuance of 3,961,810 shares of our common stock. We also have pre-funded warrants to purchase 80,956 shares of our common stock outstanding. The shares issuable upon exercise or vesting 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.

Changes in tax law could adversely affect our business or financial condition. For example, 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, as amended by the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, 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% for taxable years beginning after December 31, 2020 and limitation of the deduction for net operating losses to 80% of current year taxable income for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely). In addition, beginning in 2022, the TCJA eliminates the option to deduct research and development expenditures currently and generally requires corporations to capitalize and amortize them over five years or 15 years (for expenditures attributable to foreign research).

As part of Congress' response to the COVID-19 pandemic, in addition to the CARES Act, economic relief legislation was enacted in 2020 and 2021 containing tax provisions. The IRA, which was signed into law in August 2022, also introduced new tax provisions, including a one percent excise tax imposed on certain stock repurchases by publicly traded corporations.

Regulatory guidance under the TCJA, the IRA, and additional legislation 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 legislations, 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 such legislation.

The enactment of some or all of the recommendations set forth or that may be forthcoming in the Organization for Economic Cooperation and Development's, or OECD, project on "Base Erosion and Profit Shifting" by tax authorities in the countries in which we operate, could unfavorably impact our effective tax rate. These initiatives focus on common international principles for the entitlement to tax global corporate profits and enactment of minimum global tax rate of 15%. Many countries have or are in the process of enacting legislation intended to implement the OECD Global Anti-Base Erosion, or GloBEModel Rules effective on January 01, 2024. The impact on the Company will depend on the timing of implementation, the exact nature of each country's GloBE legislation, guidance, and regulations thereon and their application by the tax authorities either prospectively or retrospectively.

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, 2024, we had both federal and state net operating loss carryforwards of $422.5 million and $621.8 million, respectively, and federal and state research and development tax credit carryforwards of $107.8 million and $26.4 million, respectively. Federal net operating loss carryforward generated post-2017 in the amount of $420.9 million may be carried forward indefinitely. The remaining net operating loss and research and development tax credit carryforward will begin to expire in 2025. 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 13, "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 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 the Sixth Street Financing Agreement 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 28, 2025, our executive officers and directors, and entities associated or affiliated with our executive officers and directors, in the aggregate, beneficially owned shares representing approximately 16.4% of our outstanding common stock, including one of our largest stockholders, Morningside Venture Investments Ltd., which beneficially owned approximately 10.3% 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 1C. Cybersecurity.

We have certain processes for assessing, identifying and managing cybersecurity risks, which are built into our information technology function and are designed to help protect our information assets and operations from internal and external cyber threats and employee, health care professionals, or HCPs, and patient information from unauthorized access or attack, as well as secure our networks and systems. Such processes include physical, procedural and technical safeguards, response plans, regular tests on our systems, incident simulations and routine review of our policies and procedures to identify risks and improve our practices. We engage certain external parties, including consultants, independent privacy assessors, and computer security firms to enhance our cybersecurity oversight. We consider the internal risk oversight programs of third-party service providers before engaging them in order to help protect us from any related vulnerabilities.

We do not believe that there are currently any known risks from cybersecurity threats that are reasonably likely to materially affect us or our business strategy, results of operations or financial condition.

The Audit Committee of the Board of Directors provides direct oversight over cybersecurity risk. The Audit Committee receives quarterly updates from management regarding cybersecurity matters, and is notified between such updates regarding significant new cybersecurity threats or incidents.

Our Head of Information Technology leads the operational oversight of company-wide cybersecurity strategy, policy, standards and processes and works across relevant departments to assess and help prepare us and our employees, HCPs and patients to address cybersecurity risks. The Head of Information Technology cybersecurity function brings security credentials and expertise, with broad global cybersecurity and compliance experience in life science, healthcare, and federal government. In addition to our cybersecurity team, a managed security service provider provides us with additional coverage to monitor, detect and respond to threats and vulnerabilities.

In an effort to deter and detect cyber threats, we provide all employees, including part-time and temporary employees, with cybersecurity information and training, which covers timely and relevant topics, including social engineering, phishing, password protection, confidential data protection, asset use and mobile security, and educates employees on the importance of reporting all incidents immediately. Our third-party risk management program is integrated with global sourcing and procurement, and requires vendor risk assessments, incident reporting, and data protection controls. We also use technology-based tools to mitigate cybersecurity risks and to bolster our employee-based cybersecurity programs.

Item 2. Properties.

Details of our principal properties as of December 31, 2024, are provided below:

Location	Function	Size	Property Interest
Waltham, MA, USA	Corporate Headquarters	77,818 sq. ft.	Leased
San Francisco, CA, USA	Office space	5,044 sq. ft.	Leased
Zug, Switzerland	Office space	938 sq. m.	Leased
Munich, Germany	Office space	1,363 sq. m.	Subleased
Watertown, MA, USA	Lab space	9,704 sq. ft.	Leased

Item 3. Legal Proceedings.

On August 2, 2023, Judith M. Soderberg filed a putative class action in the United States District Court for the District of Delaware against the Company and certain current and former executive officers of the Company (the "Complaint"). The Complaint alleges, among other things, that the defendants violated Sections 10(b) and/or 20(a) of the Exchange Act and Rule 10b-5 promulgated thereunder by misrepresenting and/or omitting certain material facts related to the design of SYFOVRE's clinical trials and the risks associated with SYFOVRE's commercial adoption. The Complaint seeks, among other relief, compensatory damages and equitable relief in favor of the alleged class against all defendants, including interest, and reasonable costs and expenses incurred by plaintiffs, including attorneys' and expert fees.

On October 2, 2023, the defendants moved to transfer the action to the United States District Court for the District of Massachusetts.

On October 23, 2023, the Court appointed Ray Peleckas and Michigan Laborers' Pension Fund together as Co-Lead Plaintiffs and assigned the action the caption In Apellis Pharmaceuticals, Inc. Securities Litigation, Case 1:23-cv-00834-MN. The Co-Lead Plaintiffs filed an amended complaint on February 8, 2024 (the "Amended Complaint"). The Amended Complaint is brought on behalf of a class of all persons and entities who purchased or otherwise acquired Apellis common stock between January 28, 2021 and July 28, 2023, inclusive, names the Company and Cedric Francois, our chief executive officer, as defendants, and makes similar allegations, asserts the same claims and seeks the same relief as the Complaint. On May 17, 2024, the United States District Court for the District of Delaware approved the motion to transfer to the United States District Court for the District of Massachusetts. The defendants moved to dismiss the Complaint on June 12, 2024, and the Court held oral argument on this motion for November 14, 2024. The Court has not yet ruled on this motion to dismiss.

On December 19, 2024, purported stockholder Patrick Campbell, and on December 30, 2024, purported stockholder Kenneth Olson filed putative stockholder derivative lawsuits in the United States District Court for the District of Massachusetts on behalf of the Company against the Company's directors for breach of fiduciary duty, unjust enrichment, waste, and alleged violation of Section 14(a) of the Exchange Act related to the design of SYFOVRE's clinical trials and the risks associated with SYFOVRE's commercial adoption. The complaints seek monetary and punitive damages, and costs, including attorneys' fees. On January 21, 2025, the cases were consolidated under the caption *In re Apellis Pharmaceuticals, Inc. Derivative Litigation*, No. 1:24-cv-13128-JEK. By the same order, the Court stayed the stockholder derivative litigation pending the Court's ruling on the defendants' motion to dismiss in the securities class action.

The Company's businesses may also be subject at any time to other commercial disputes, product liability claims, personal injury claims, third-party subpoenas or various other lawsuits arising in the ordinary course of business, including intellectual property infringement, employment or investor matters, and the Company expects that this will continue to be the case in the future.

For example, in August 2024, an individual filed a civil action against the Company in the United States District Court in the Northern District of Texas, alleging personal injury claims in connection with the use of SYFOVRE. We moved to dismiss this civil action in September 2024. The Court has not yet ruled on this motion to dismiss, as of the date of issuance of these consolidated financial statements.

The outcome of the matters described above cannot be predicted with certainty and therefore any loss is neither probable nor reasonably estimable. However, the Company intends to vigorously defend against these matters.

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 19, 2025, we had 2 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, the Sixth Street Financing Agreement 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.

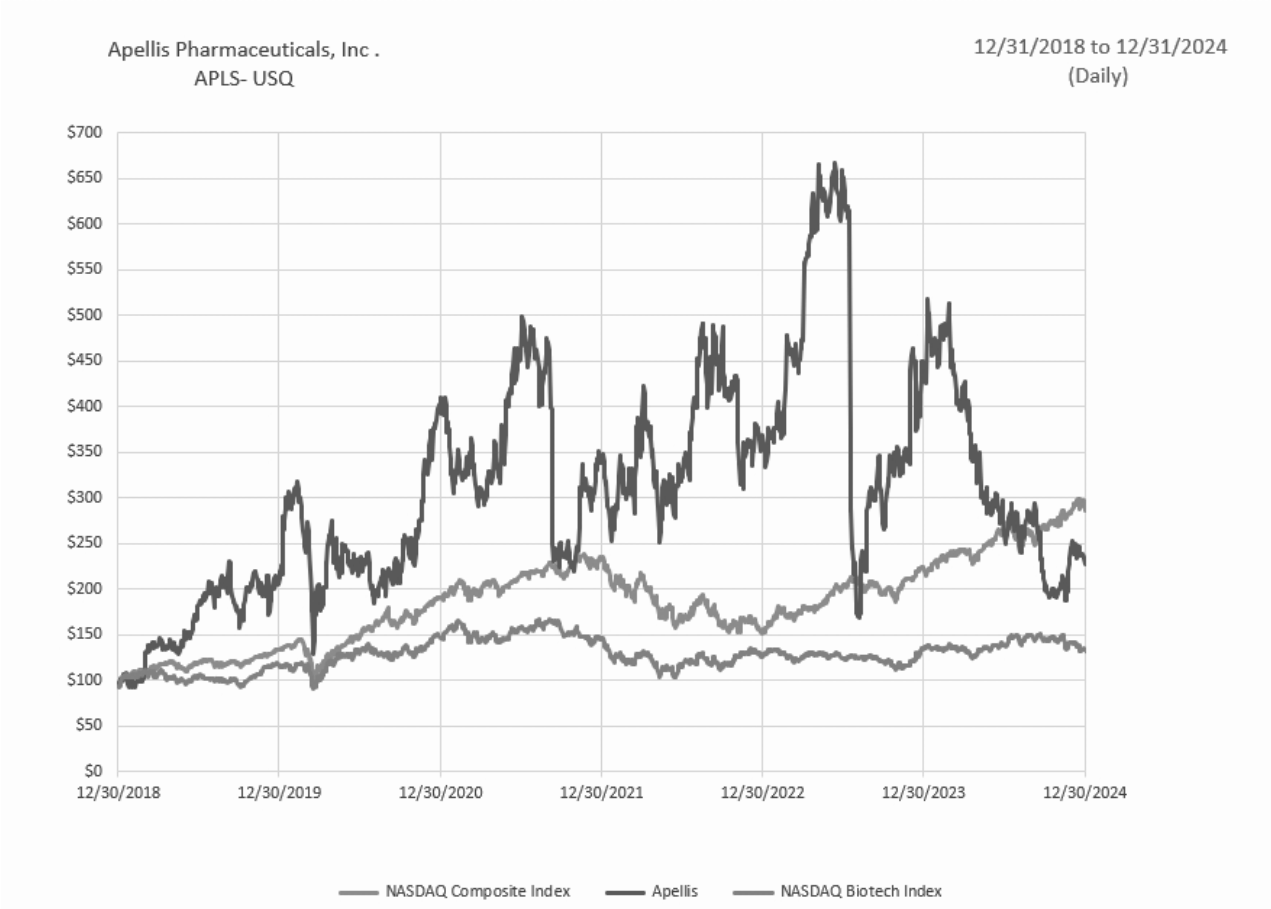
Securities Authorized for Issuance under Equity Compensation Plans

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 December 30, 2018 and December 31, 2024, 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 December 31, 2018 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. 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. We believe that this approach has the potential to effectively control diseases with high unmet need and that are driven by excessive complement activation. We currently have two marketed drugs that target C3, the central protein in the complement cascade: SYFOVRE (pegcetacoplan injection), approved by the U.S. Food and Drug Administration, or FDA, in February 2023 for the treatment of geographic atrophy secondary to age-related macular degeneration, or GA; and EMPAVELI (pegcetacoplan), approved by the FDA in May 2021 for the treatment of paroxysmal nocturnal hemoglobinuria, or PNH.

We believe SYFOVRE has the potential to be the standard of care for patients with GA, a disease that affects an estimated 1.5 million people in the United States. While we have exclusive, worldwide commercialization rights for intravitreal pegcetacoplan, we intend to focus our commercialization efforts in the U.S. and explore international expansion in select markets, including Australia, where we received marketing approval in January 2025. For the year ended December 31, 2024, and 2023, we generated $611.9 million and $275.2 million in U.S. net product revenue from sales of SYFOVRE. We are also developing a next-generation therapy by combining SYFOVRE treatment with APL-3007, which is a small interfering RNA, or siRNA, aimed at comprehensively blocking complement activity in the retina and the choroid. We plan to initiate a Phase 2 multi-dose trial in patients with GA in the second quarter of 2025.

We believe that EMPAVELI has the potential to be a best-in-class treatment for a range of indications with high unmet needs. We have exclusive U.S. commercialization rights for EMPAVELI, and our collaboration partner, Swedish Orphan Biovitrum AB (Publ), or Sobi, has exclusive ex-U.S. commercialization rights for systemic pegcetacoplan outside of the United States. For the years ended December 31, 2024 and 2023, we generated $98.1 million and $91.0 million, respectively, in U.S. net product revenue from sales of EMPAVELI for PNH and received $18.4 million and $10.0 million, respectively, in royalties from our collaboration partner, Swedish Orphan Biovitrum AB (Publ), or Sobi, which has exclusive ex-U.S. commercialization rights for systemic pegcetacoplan outside of the United States. We have commercialization rights for systemic pegcetacoplan in the United States.

The next indications we are pursuing with EMPAVELI are C3 glomerulopathy, or C3G, and primary immune complex membranoproliferative glomerulonephritis, or IC-MPGN, which together affect an estimated 5,000 people in the United States. We submitted a supplemental new drug application, or sNDA, to the FDA in early 2025, following the positive results from the Phase 3 VALIANT trial investigating systemic pegcetacoplan in adolescent and adult patients with naive and post-transplant recurrence C3G and IC-MPGN that we reported in August 2024. Importantly, the VALIANT study demonstrated positive effects on the three key markers of disease at six months: a 68% reduction in proteinuria in C3G and IC-MPGN patients compared to placebo ($p < 0.0001$), the primary endpoint. Results were consistent across all subgroups, including disease type, age, and transplant status. Additionally, pegcetacoplan-treated patients achieved stabilization of kidney function (nominal $p=0.03$), as measured by estimated glomerular filtration rate, and a substantial proportion of patients achieved a reduction in C3c staining intensity (nominal $p<0.0001$). Data also demonstrated favorable safety and tolerability results, consistent with pegcetacoplan's established profile. Additionally, in February 2025, Sobi received validation for its indication extension application for C3G and IC-MPGN from the European Medicines Agency, or EMA.

We plan to initiate two new Phase 3 clinical trials with EMPAVELI in the second half of 2025 for the treatment of primary focal segmental glomerulosclerosis, or FSGS, and delayed graft function, or DGF. Both FSGS and DGF are both rare, severe nephrology conditions with no approved therapies and in which complement overactivation plays a significant role. Sobi is also leading the development of systemic pegcetacoplan for hematopoietic stem cell transplantation-associated thrombotic microangiopathy, or HSCT-TMA, in hematology under the collaboration.

Finally, we are developing new product candidates to further advance our pipeline. Through our collaboration with Beam Therapeutics, Inc., or Beam, we have commenced pre-clinical studies for a treatment targeting the neonatal Fc receptor, orFcRn, which has the potential to be a first-in-class gene editing treatment for future target indications with one-time dosing. We are also developing other programs with our proprietary in-house capabilities.

To date, we have financed our operations primarily through approximately $2.6 billion in net proceeds from public and private offerings of our common stock and convertible securities, $401.5 million in payments and royalties from Sobi pursuant to our

collaboration agreement, $532.5 million under various credit arrangements, including with Sixth Street Lending Partners, or Sixth Street, and SFJ Pharmaceuticals Group, or SFJ, and $98.8 million relating to the unwinding of certain capped call transactions in March 2024, as well as from the proceeds of our operations. To date, we have exchanged $425.4 million and converted $0.7 million of aggregate principal amount of our Convertible Notes for shares of our common stock. Our non-dilutive financing activities, which include the Sixth Street Financing Agreement (as defined below), the repayment of our remaining obligations to SFJ and the partial unwinding of our capped call transactions, increased the amount of cash available to us through 2025 by approximately $270.0 million, with the potential for us to access additional short-term liquidity through a second draw of $100.0 million under the Credit Facility (as defined below).

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. Our net losses were $197.9 million, $528.6 million, and $652.2 million for the years ended December 31, 2024, 2023 and 2022, respectively. As of December 31, 2024, we had an accumulated deficit of $3.0 billion.

Our operating results may fluctuate significantly from quarter to quarter and year to year. We anticipate that we will continue to incur significant commercialization expenses related to sales, marketing, medical affairs, manufacturing, distribution and other commercial infrastructure associated with the commercialization of EMPAVELI for the treatment of PNH and other indications and the commercialization of SYFOVRE for the treatment of GA. In addition, we expect to continue to incur these expenses 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.

Financing Agreement and Credit Facility

On May 13, 2024, we entered into a financing agreement, or the Sixth Street Financing Agreement, with certain of our material subsidiaries as guarantors party thereto, the lenders party thereto, or the Lenders, and Sixth Street Lending Partners, as the administrative agent and collateral agent for the Lenders.

The Sixth Street Financing Agreement provides for a senior secured term loan facility of up to $475.0 million, or the Credit Facility, consisting of an initial draw of $375.0 million at closing and a potential additional $100.0 million draw at our option upon satisfaction of a $50.0 million minimum cash requirement and a requirement that our trailing three-month sales of SYFOVRE is at least $180.0 million prior to the $100.0 million draw. We can exercise the option for the additional $100.0 million draw through September 30, 2025, assuming such requirements are met.

The Credit Facility matures on May 13, 2030 (the "Maturity Date") and bears interest at (i) in the case of SOFR Loans, an annual rate equal to 3-month Term SOFR (subject to 1.00% floor), plus 5.75%, and (ii) in the case of Base Rate Loans, an annual rate equal to the base rate as defined in the agreement (subject to 2.00% floor), plus 4.75%. Certain additional commitment and undrawn amount fees are also payable in connection with the Credit Facility.

The net proceeds from the initial draw of the Credit Facility were approximately $358.2 million, net of $16.8 million of issuance costs. We used the majority of the proceeds of the $375.0 million draw at closing to buy out our remaining obligations to SFJ, in the amount of approximately $326.5 million.

The Credit Facility does not provide for scheduled amortization payments during the term. All principal will be due on the Maturity Date. We have the right to prepay loans under the Credit Facility at any time. We are required to repay loans under the Credit Facility with proceeds from certain asset sales, condemnation events and extraordinary receipts, subject, in some cases, to reinvestment rights. Repayments are subject to a prepayment premium. Repayments may be made after the first year of the loan and are subject to a prepayment premium up to 3% depending on timing.

All obligations under the Sixth Street Financing Agreement are secured on a first-priority basis, subject to certain exceptions, by security interests in substantially all of our assets and assets of our material subsidiaries, including our intellectual property, and are guaranteed by our material subsidiaries, including foreign subsidiaries, subject to certain exceptions.

The Sixth Street Financing Agreement contains customary covenants, including, without limitation, a financial covenant to maintain liquidity of at least $50.0 million if our market capitalization is below $3.0 billion, and negative covenants that, subject to

certain exceptions, restrict indebtedness, liens, investments (including acquisitions), fundamental changes, asset sales and licensing transactions, dividends, modifications to material agreements, payment of subordinated indebtedness, and other matters customarily restricted in such agreements. Among other permissions, we are permitted, on terms and conditions set forth on the Sixth Street Financing Agreement, to enter into a separate asset-based financing arrangement with a third party in an amount of up to $100.0 million, which amount is increased to $200.0 million upon certain sales or market capitalization thresholds, and to have outstanding convertible unsecured notes in an amount equal to the greater of $400.0 million and 10% of our market capitalization, but not to exceed $600.0 million. We are subject to restrictions on sales and licensing transactions with respect to our core intellectual property, defined to include SYFOVRE, EMPAVELI, and other pegcetacoplan product assets, subject to certain exceptions, including certain transactions related to areas outside the United States and Europe.

The Sixth Street Financing Agreement also contains certain events of default after which loans under the Credit Facility may be due and payable immediately, including payment defaults, material inaccuracy of representations and warranties, covenant defaults, bankruptcy and insolvency proceedings, cross-defaults to certain other agreements, judgments against us and our subsidiaries, and change of control.

SFJ Agreement

In 2019, we entered into a development funding agreement (as amended, the "SFJ agreement") with SFJ Pharmaceuticals Group ("SFJ"), under which SFJ agreed to provide funding to us to support the development of pegcetacoplan for the treatment of patients with PNH. Under the SFJ agreement, SFJ paid us an aggregate of $140.0 million between June 2019 and January 2020.

Following regulatory approval for the use of systemic pegcetacoplan as a treatment for PNH by the FDA in May 2021 and by the EMA in December 2021, we became obligated to pay SFJ an aggregate of $460.0 million in payments between 2021 and 2027. We paid SFJ an aggregate of $94.0 million through March 31, 2024.

On May 13, 2024, we used proceeds from the Sixth Street Financing Agreement to buy out our remaining obligations owed to SFJ, in the amount of approximately $326.5 million. The buyout of the SFJ development liability eliminated the remaining $366.0 million in payments to SFJ, including a total of approximately $200.0 million payable in 2024 and 2025.

Convertible Notes

On September 16, 2019, we completed a private offering of convertible notes, or the 2019 Convertible Notes, with an aggregate principal amount of $220.0 million issued pursuant to an indenture, or the Indenture, with U.S. Bank National Association, as 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. We used $28.4 million of the net proceeds from the sale of the 2019 Convertible Notes to pay the cost of the capped call transactions in September 2019 described below.

On May 12, 2020, we issued convertible notes, or 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. We 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 2019 Convertible Notes and the 2020 Convertible Notes are referred to together as the Convertible Notes. The Convertible Notes are our senior unsecured obligations and bear interest at a rate of 3.5% per year payable semiannually in arrears on March 15 and September 15 of each year, beginning on March 15, 2020. The Convertible Notes will mature on September 15, 2026, unless converted earlier, redeemed or repurchased in accordance with their terms.

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.

The conditional conversion feature of the Convertible Notes was not triggered as of December 31, 2024.

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 regardless of the foregoing circumstances. 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.

As of September 20, 2023, we may redeem for cash all or a portion of the Convertible Notes, at our option, 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 call any Convertible Notes for redemption, it will constitute a "make-whole fundamental change" with respect to such Convertible Notes, in which case the conversion rate applicable to the conversion of such Notes, if converted in connection with the redemption, will be increased in certain circumstances. We have not called for redemption any of the Convertible Notes as of December 31, 2024.

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 notes to be repurchased, plus any accrued and unpaid interest to, but excluding, the fundamental change repurchase date.

In January 2021, July 2021 and July 2022, we entered into separate, privately negotiated exchange agreements to modify the conversion terms with certain holders of our Convertible Notes. Under the terms of these exchange agreements, in January 2021, July 2021 and July 2022, the holders exchanged approximately $126.1 million of 2019 Convertible Notes, $201.1 million of 2019 Convertible Notes and 2020 Convertible Notes, and $98.1 million of 2020 Convertible Notes, respectively, in aggregate principal amount held by them for an aggregate of 3,906,869 shares, 5,992,217 shares and 3,027,018 shares, respectively, of common stock we issued. In accordance with FASB ASC Topic 470-20, "Debt – Debt with Conversion and Other Options," or 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.

The conditional conversion feature of the Convertible Notes was triggered as of December 31, 2023, and as a result the Convertible Notes were convertible at the option of the holders until March 31, 2024. No Convertible Notes were converted during this period.

The conditional conversion feature of the Convertible Notes was not triggered as of December 31, 2024.

As of December 31, 2024 we held in treasury Convertible Notes in principal amount of $425.4 million which notes had not been cancelled.

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 $63.14, 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 Sobi collaboration agreement, 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. 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 Sobi collaboration 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 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. Since contract inception, we have recognized $65.0 million in contra-research and development expenses and waived the remaining $15.0 million in connection with the decision to discontinue the CAD program.

The European Commission approved systemic Aspaveli (pegcetacoplan) for the treatment of adults with PNH in December 2021. In March 2022, we earned a $50.0 million payment from Sobi related to the first regulatory and reimbursement milestone in Europe, which we received in April 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.

Financial Operations Overview

Revenue

Our revenues consist of product sales of EMPAVELI and SYFOVRE, and revenues derived from our collaboration arrangement with Sobi.

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

Product revenue is derived from our sales of our commercial products, EMPAVELI and SYFOVRE, in the United States.

Licensing and Collaboration Revenue

Licensing and other revenue is derived from our 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.

Cost of Sales

Cost of sales consists primarily of costs associated with the manufacturing of EMPAVELI and SYFOVRE, royalties owed to our licensor for such sales, and certain period costs.

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 by program.

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 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.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of employee-related expenses including salaries, bonuses, benefits and share-based compensation, consulting and professional fees, marketing and advertising costs, medical affairs and regulatory costs associated with our commercial products, 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. Marketing and advertising costs include marketing literature, promotional activities, conferences and seminars, branding and sponsorships.

We anticipate that our selling, 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 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

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 the variable considerations with critical accounting estimates:

Returns: Consistent with industry practice, we offer 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. 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 have visibility into the inventory distribution channel, we are 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 (to the extent available) and the underlying product demand.

GPO Rebates: Commercial rebates are based on (i) our estimates of end-user purchases through a GPO, (ii) the corresponding contractual rebate percentage tier we expect each GPO to achieve, and (iii) our estimates of the impact of any prospective rebate program changes made by us.

Credit Card Fees: SDs will sell downstream to customers who may pay for product via credit card. The Company will reimburse its SDs for the credit card fees incurred as a result of SDs accepting credit cards as a form of payment from the downstream customers. Credit card fees are recorded as an offset to revenue based on the average aggregate credit card rate as a percentage of SD sales at the time revenue from the sale is recognized.

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, labor, overhead, and freight. We perform an assessment of the recoverability of capitalized inventory during each reporting period, and write down any excess and obsolete inventories to their estimated realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, are recorded within cost of sales. The determination of whether inventory costs will be realizable requires estimates by management. Provisions for potentially obsolete or slow-moving inventory, are made based on the Company's analysis of product dating, inventory levels, historical obsolescence and future sales forecasts. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required which would be recorded as a cost of sales in the consolidated statements of operations and comprehensive loss.

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.

Results of Operations

Comparison of Years Ended December 31, 2024 and 2023

The following table summarizes our results of operations for the years ended December 31, 2024 and 2023, together with the dollar increase or decrease and percentage change in those items:

(in thousands)	Year Ended December 31, 2024	Year Ended December 31, 2023	Change $	Change %
Revenue:				
Product Revenue, net	$ 709,954	$ 366,281	$ 343,673	94%
Licensing and other revenue	71,413	30,310	41,103	136%
Total revenue:	781,367	396,591	384,776	97%
Operating expenses:				
Cost of sales	117,723	58,510	59,213	101%
Research and development	327,570	354,387	(26,817)	(8%)
Selling, general and administrative	501,053	500,815	238	0%
Total operating expenses	946,346	913,712	32,634	4%
Net operating loss	(164,979)	(517,121)	352,142	(68%)
Loss on extinguishment of development liability	(1,949)	—	(1,949)	(100%)
Interest income	12,773	20,933	(8,160)	(39%)
Interest expense	(40,391)	(29,581)	(10,810)	37%
Other expense, net	(2,170)	(727)	(1,443)	198%
Net loss before taxes	(196,716)	(526,496)	329,780	(63%)
Income tax expense	1,162	2,132	(970)	(45%)
Net loss	$ (197,878)	$ (528,628)	$ 330,750	(63%)

Product Revenue, Net

Our product revenue, net is derived from sales of EMPAVELI and SYFOVRE sales in the United States. We recognized $710.0 million and $366.3 million of net product revenue as of December 31, 2024 and 2023, respectively. The net product revenue of $710.0 million for the year ended December 31, 2024, consists of $98.1 million in net product revenue from sales of EMPAVELI and $611.9 million in net product revenue from sales of SYFOVRE. The net product revenue of $366.3 million for the year ended December 31, 2023, consists of $91.0 million in net product revenue from sales of EMPAVELI and $275.2 million in net product revenue from sales of SYFOVRE.

Licensing and Other Revenue

Licensing and other revenue was $71.4 million and $30.3 million for the year ended December 31, 2024 and 2023, respectively. Licensing and other revenue of $71.4 million for the year ended December 31, 2024 consisted of $53.0 million in revenue from product supplied to Sobi, and $18.4 million in royalty revenue from Sobi. Licensing and other revenue of $30.3 million for the year ended December 31, 2023 consisted of $10.0 million in revenue from product supplied to Sobi, $15.3 million in royalty revenue from Sobi and $5.0 million from collaboration with Sobi.

Cost of Sales

Cost of sales was $117.7 million and $58.5 million for the year ended December 31, 2024 and 2023, respectively. The increase in cost of sales was primarily driven by a $6.1 million increase due to higher volume from commercial sales and product provided under our patient assistance programs, a $27.4 million increase due to higher volume of product supplied to Sobi, a $6.0 million increase in royalty expense, a $11.7 million increase in expenses incurred related to excess, obsolete or scrapped inventory, and $8.0 million incurred in connection with the termination of minimum purchase obligations.

In addition, prior to receiving FDA approval for EMPAVELI on May 14, 2021, the costs associated with the manufacture of EMPAVELI inventory were expensed as incurred as research and development expense. This resulted in inventory being sold during the years ended December 31, 2024 and 2023 for which a portion of the costs had been previously expensed prior to FDA approval. We expect this to continue to impact the cost of sales as the remaining pre-FDA inventory is sold to customers. As of December 31, 2024 and 2023, respectively, the remaining pre-FDA approved inventory was $19.5 million and $26.3 million, which primarily consisted of raw materials.

Research and Development Expenses

The following table summarizes our research and development expenses incurred during the years ended December 31, 2024 and 2023, together with the dollar increase or decrease and percentage change in those items:

(In thousands)	**Year Ended December 31,**		**Change**	**Change**
	2024	**2023**	**$**	**%**
Program-specific external costs:				
PNH	$ 17,879	$ 19,504	$ (1,625)	(8%)
C3G & IC-MPGN	34,507	36,160	(1,653)	(5%)
ALS	824	9,378	(8,554)	(91%)
CAD	21,037	7,115	13,922	196%
HSCT-TMA	2,612	2,842	(230)	(8%)
GA	59,134	52,078	7,056	14%
Other development and discovery programs	51,463	52,733	(1,270)	(2%)
Total program-specific costs	187,456	179,810	7,646	4%
Unallocated external costs				
Non-program specific external costs	6,966	7,002	(36)	(1%)
Total unallocated external costs	6,966	7,002	(36)	(1%)
Unallocated internal costs				
Compensation and related personnel costs	128,029	162,515	(34,486)	(21%)
Other expenses	5,119	5,060	59	1%
Total unallocated internal costs	133,148	167,575	(34,427)	(21%)
Total research and development costs	$ 327,570	$ 354,387	$ (26,817)	(8%)

Research and development expenses decreased by $26.8 million to $327.6 million for the year ended December 31, 2024 from $354.4 million for the year ended December 31, 2023, a decrease of 8%. The decrease in research and development expenses was primarily attributable to a $34.5 million decrease in compensation and related personnel costs, which was partially offset by a $7.6 million increase in program specific external costs.

The increase in our program-specific external costs of $7.6 million was driven by an increase of $13.9 million as a result of a $15.0 million one-time expense related to the discontinuation of the CAD program and an increase of $7.1 million in GA costs related to development and pre-clinical programs. These increases were partially offset by a $1.7 million decrease related to C3G and IC-MPGN costs, a $1.6 million decrease in PNH, a $8.6 million decrease in ALS costs due to the discontinuation of the Phase 2 MERIDIAN study, and a $1.3 million decrease in other development and discovery program costs.

The decrease in compensation and related personnel costs of $34.5 million was driven by a $32.8 million decrease in salaries and benefits due to lower headcount compared to the prior year and a $1.7 million decrease in share-based compensation expense.

Selling, General and Administrative Expenses

Selling, general and administrative expenses increased by $0.3 million to $501.1 million for the year ended December 31, 2024, from $500.8 million for the year ended December 31, 2023. The increase was primarily attributable to an increase of $2.1 million in office expenses, an increase of $1.7 million in factoring fees, an increase of $1.2 million in travel expenses, and an increase of $1.5 million in insurance expenses, which were partially offset by a decrease of $4.6 million in professional and consulting fees and a decrease in personnel related costs of $1.7 million. The decrease in personnel related costs of $1.7 million consisted of a $0.7 million decrease in recruiting expenses and a $10.6 million decrease in salaries and benefits, partially offset by a $9.7 million increase in share-based compensation expense.

Loss on extinguishment of development liability

We paid our remaining obligations under the SFJ agreement in full in May 2024. We concluded that the development liability was extinguished as of the payoff date. The difference of $1.9 million between the reacquisition price of $326.5 million and the net carrying value of the development liability of $324.6 million was recorded as a loss on the extinguishment of the development liability as of December 31, 2024.

Interest Income

Interest income was $12.8 million for the year ended December 31, 2024, a decrease of $8.1 million, compared to $20.9 million for the year ended December 31, 2023. The decrease in interest income was primarily attributable to decreased investments and a decline in money market rates during the year ended December 31, 2024.

Interest Expense

Interest expense was $40.4 million for the year ended December 31, 2024, an increase of $10.8 million, compared to $29.6 million for the year ended December 31, 2023. The increase is primarily due to the interest incurred under the Credit Facility and was partially offset by a decrease in the balance of the development liability.

Other (Expense)/ Income, Net

Other expense was $2.2 million for the year ended December 31, 2024 as compared to other expense of $0.7 million for the year ended December 31, 2023. The increase was primarily due to foreign currency revaluation losses.

Income Tax Expense

Income tax expense was $1.2 million for the year ended December 31, 2024 as compared to $2.1 million for the year ended December 31, 2023. The decrease is primarily due to state taxes.

Comparison of the Years Ended December 31, 2023 and 2022

A discussion of changes in our results of operations during the year ended December 31, 2023 compared to the year ended December 31, 2022 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, 2023, filed with the SEC on February 27, 2024, as amended by Amendment No. 1 thereto filed with the SEC on February 29, 2024 (the "2023 Form 10-K"), 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 approximately $2.6 billion in net proceeds from public and private offerings of our common stock and convertible securities, $401.5 million in payments and royalties from Sobi pursuant to our collaboration agreement, $532.5 million under various credit arrangements, including with Sixth Street and SFJ, and $98.8 million relating to the unwinding of the capped call transactions in March 2024, as well as from the proceeds of our operations.

In May 2024, we entered into the Sixth Street Financing Agreement, which provides for the Credit Facility, consisting of an initial draw of $375.0 million at closing and a potential additional $100.0 million draw at our option upon satisfaction of a $50.0 million minimum cash requirement and a requirement that our trailing three-month sales of SYFOVRE is at least $180.0 million prior to the $100.0 million draw. The Credit Facility matures on May 13, 2030 and bears interest at an annual rate equal to the 3-month Secured Overnight Financing Rate (SOFR) + 5.75% (subject to 1.00% floor). Certain additional commitment and undrawn amount fees are also payable in connection with the Credit Facility. We used the majority of the proceeds of the $375.0 million draw at closing to buy out our remaining obligations owed to SFJ, in the amount of approximately $326.5 million.

We are permitted under the Sixth Street Financing Agreement to enter into a separate asset-based financing arrangement with a third party in an amount of up to $100.0 million, which amount is increased to $200.0 million upon certain sales or market

capitalization thresholds, and to have outstanding convertible unsecured notes in an amount equal to the greater of $400.0 million and 10% of our market capitalization, but not to exceed $600.0 million.

In August 2024, the Company entered into an agreement (the "Factoring Agreement") to sell certain accounts receivable to a third-party financial institution at a discount to the face value of the accounts receivable. Under the Factoring Agreement, the maximum amount of outstanding accounts receivables sold at any time is $100.0 million.

In November 2023, we entered into a sales agreement, or the sales agreement, with Cowen and Company, LLC, or Cowen, as agent, pursuant to which we may offer and sell shares of our common stock having an aggregate offering from of up to $300.0 million from time to time. Any sales made under the sales agreement will be made at market prices by any method that is deemed to be an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933. Any sales under the sales agreement will be made pursuant to our registration statement on Form S-3, which became effective on February 22, 2023. We agreed to pay Cowen compensation of up to 3.0% of the gross proceeds of the sale of shares made under the sales agreement. We did not make any sales under the sales agreement during the year ended December 31, 2024.

In February 2023, we issued and sold 4,007,936 shares of our common stock and, in lieu of common stock to investors who so chose, pre-funded warrants to purchase 2,380,956 shares of our common stock in a follow-on offering, including 833,333 shares sold pursuant to the underwriters’ exercise in full of their option to purchase additional shares of common stock. The price to the public of the shares of common stock was $63.00 per share and the price to the public of the pre-funded warrants was $62.9999 per pre-funded warrant. The pre-funded warrants have an exercise price equal to $0.0001 per share and do not expire. The pre-funded warrants were accounted for as equity instruments. We received total net proceeds of $384.4 million, after deducting underwriting discounts and commissions of $18.8 million and offering cost of $0.3 million. For the period ended December 31, 2024 2,299,991 shares of common stocks were issued from the exercise of pre-funded warrants. As of December 31, 2024, pre-funded warrants to purchase 80,956 shares of our common stock were still outstanding.

In February 2024, we entered into agreements with the capped call counterparties to unwind a portion of the capped call transactions. The unwind agreements applied to the portion of the capped call transactions in a notional amount corresponding to the $426.1 million principal amount of Convertible Notes that we held in treasury as of December 31, 2024 or have been previously converted. The unwind transactions were settled at volume-weighted average price per share of $64.11, which resulted in cash proceeds to us of $98.8 million. As of December 31, 2024, the remaining capped call transactions had a notional amount corresponding to $93.9 million principal amount of Convertible Notes.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2024 and 2023:

(in thousands)	**Year Ended December 31,**	
	2024	**2023**
Net cash used in operating activities	$ (87,866)	$ (594,735)
Net cash used in investing activities	(403)	(674)
Net cash provided by financing activities	149,241	394,499
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(659)	135
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 60,313	$ (200,775)

Net Cash Used in Operating Activities

Net cash used in operating activities was $87.9 million for the year ended December 31, 2024 and consisted primarily of a net loss of $197.9 million adjusted for $128.4 million of non-cash items, including share-based compensation expense of $114.1 million, depreciation expense of $1.8 million, loss on extinguishment of development liability of $1.9 million and accretion of discount to the development liability of $8.9 million. Further, it included a net increase in operating assets and liabilities of $18.4 million, which was driven by an increases in accounts receivable of $58.5 million, an increase in inventory of $10.8 million, a decrease in prepaid assets of $20.4 million, a decrease in other current assets of $10.8 million, an increase in accounts payable of $1.1 million, and an increase in accrued expenses of $18.2 million. The change in accounts receivable was primarily driven by the derecognition of certain accounts receivable under our Factoring Agreement.

Net cash used in operating activities was $594.7 million for the year ended December 31, 2023 and consisted primarily of a net loss of $528.6 million adjusted for $134.1 million of non-cash items, including share-based compensation expense of $105.9 million, depreciation expense of $1.8 million, accretion of discount to the development liability of $26.0 million and accretion of discounts for

convertible debt of $0.3 million. Further, it included a net increase in operating assets of $200.2 million, which was driven by increases in accounts receivable of $198.7 million, an increase in inventory of $60.6 million, and an increase in prepaid assets of $1.9 million, which was partially offset by an increase in accounts payable and accrued expenses of $35.1 million and a decrease in other assets of $25.9 million.

Net Cash Used in Investing Activities

Net cash used in investing activities during the year ended December 31, 2024 was $0.4 million due primarily to purchases of fixed assets.

Net cash used in investing activities during the year ended December 31, 2023 was $0.7 million due primarily to purchases of fixed assets and partially offset by proceeds from the sale of fixed assets.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $149.2 million during the year ended December 31, 2024 and consisted primarily of net proceeds from the initial draw of the Credit Facility of $358.2 million, the settlement of capped call unwind transactions of $98.8 million, $14.3 million of proceeds from the exercise of stock options and $4.5 million of proceeds from the issuance of our common stock under the employee stock purchase plan, partially offset by repayment of $326.5 million for the development liability.

Net cash provided by financing activities was $394.5 million during the year ended December 31, 2023 and consisted primarily of proceeds from the follow-on common stock and pre-funded warrant offering in March 2023 of $384.4 million, $71.3 million proceeds upon the exercise of stock options and $5.4 million proceeds from the issuance of our common stock under the employee stock purchase plan, partially offset by payments of $55.5 million for the development liability as well as the payments of employee tax withholding related to equity-based compensation of $11.0 million.

Funding Requirements

We expect to continue incur expenses to support our ongoing commercial activities related to product manufacturing, marketing, sales and distribution of EMPAVELI for PNH and SYFOVRE for GA. In addition, we expect to continue to incur expenses as we prioritize the ongoing development of systemic pegcetacoplan and focus our research initiatives on high potential opportunities.

Together with the cash that we anticipate will be generated from sales of EMPAVELI and SYFOVRE, we expect that our current cash and cash equivalents will be sufficient to fund our projected operating expenses and capital expenditure requirements for at least the next 12 months, as well as our anticipated longer-term cash requirements and obligations. Our expectations regarding our short-term and long-term funding requirements are based on assumptions that may prove to be wrong, and we may need additional capital resources to fund our operating plans and capital expenditure requirements.

We are devoting substantial resources to the commercial infrastructure for SYFOVRE for GA. We are also devoting substantial resources to the development of our product candidates. Because of the numerous risks and uncertainties associated with the commercialization of EMPAVELI and SYFOVRE and development of other product candidates, and because the extent to which we may enter into collaborations with third parties for any of these activities is unknown, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with the research, development and commercialization. Our future funding requirements and long-term capital requirements will depend on many factors, including:

- our ability to continue to successfully commercialize and sell EMPAVELI and SYFOVRE in the United States;
- the cost of and our ability to obtain regulatory approvals of SYFOVRE outside of the United States and continue to build a commercial infrastructure for SYFOVRE 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 continued commercialization of EMPAVELI, SYFOVRE 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, SYFOVRE 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 public health crises, including pandemics and epidemics, 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 and SYFOVRE in the United States or any other product we commercialize; and
- the costs of operating as a public company.

If our cash and cash equivalents, and cash generated from sales of EMPAVELI and SYFOVRE are not sufficient to fund our planned expenditures, we will need to finance our cash needs through external sources of funds, which may include equity offerings, debt financings, collaborations, strategic alliances or licensing arrangements. We currently do not have any committed external source of funds.

If we are unable to generate sufficient funds from sales of EMPAVELI and SYFOVRE, or 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.

Contractual Obligations

The following table summarizes our significant contractual obligations as of payment due date by period at December 31, 2024:

(In thousands)	Payments Due by Period				
	Total	Less than 1 Year	1-3 Years	3-5 Years	More than 5 Years
Credit Facility (1)	$ 595,778	$ 42,102	$ 84,205	$ 84,320	$ 385,151
Convertible notes (2)	99,511	3,286	96,225	—	—
Non-cancellable purchase commitments (3)	56,489	54,089	1,400	1,000	—
Operating leases (4)	18,307	7,468	9,427	1,412	—
Total	$ 770,085	$ 106,945	$ 191,257	$ 86,732	$ 385,151

(1) Amounts include interest on the credit facility outstanding as of December 31, 2024, applying contractual interest rate and assuming scheduled payments are paid as contractually required through maturity.

(2) Amounts include interest on long-term debt obligations under the debt outstanding as of December 31, 2024, applying contractual fixed interest rate and assuming scheduled payments are paid as contractually required through maturity.

(3) Amounts include our obligations under supply agreements with Bachem and NOF as of December 31, 2024 and obligations under supply agreements with other vendors.

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

We 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 are a party to a license agreement with Penn for an exclusive, worldwide license to specified patent rights in the ophthalmic field of use. We are 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, we are obligated to pay a specified portion of income we receive from sublicensees.

In April 2023, we paid $2.3 million for the achievement of a regulatory milestone as a result of the FDA approval of SYFOVRE in February 2023. In 2023, we incurred $5.0 million as a result of the achievement of sales milestones for SYFOVRE of which we paid $2.0 million in October 2023 and the remaining $3.0 million in January 2024.

As of December 31, 2024 and 2023 respectively, we have incurred royalty expense of $19.8 million and $8.9 million on sales of SYFOVRE, which is included in cost of sales on the consolidated statements of operations and comprehensive loss.

In addition, we are a party to a license agreement with Penn for an exclusive, worldwide license to specified patent rights for the development and commercialization of products in nonophthalmic fields of use, as defined therein. We are 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 us to pay low single digit royalties based on net sales of each licensed product, subject to minimum quarterly royalty thresholds. In addition, we are obligated to pay a specified portion of income we receive from sublicensees.

In January 2021, we paid $25.0 million for a sublicense fee owed to Penn related to the Sobi collaboration agreement and another licensing transaction. In August 2021, we paid $1.0 million to Penn upon the achievement of a development milestone, net of a credit for the annual license maintenance payment. In June 2022, we paid an additional $5.0 million to Penn as a sublicense fee upon the achievement of a development milestone under the Sobi collaboration. In January 2023, we paid $1.0 million to Penn upon the achievement of a sales milestone for EMPAVELI in 2022. In January 2024, we paid $0.5 million for a sublicense fee owed to Penn related to Sobi obtaining regulatory approval in Japan. Additionally, in January 2024, we paid $1.5 million as a result of the achievement of a sales milestone for EMPAVELI and Aspaveli.

As of December 31, 2024, 2023 and 2022, we have incurred royalty expense of $6.4 million, $4.8 million and $2.7 million, respectively, on sales of EMPAVELI and Aspaveli, which is included in cost of sales on the consolidated statements of operations and comprehensive loss.

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.

We have certain non-cancelable purchase obligations related to the manufacturing of drug substance and drug product. We have agreed to purchase from Bachem Americas, Inc. a significant portion of its requirements for the pegcetacoplan drug substance. Under a commercial supply agreement with NOF Corporation ("NOF"), we have agreed to purchase activated polyethylene glycol derivative, or PEG, which is a component of pegcetacoplan. In September 2024, we terminated the minimum purchase obligation with NOF for 2025. Under these agreements, as of December 31, 2024 we are obligated to pay up to an aggregate of $45.7 million to these vendors. As a result of this termination, the Company incurred an expense of $6.4 million, which is included in cost of sales on the consolidated statements of operations and comprehensive loss. As the amount is not due until January 2026, it is included in other liabilities on the consolidated balance sheet as of December 31, 2024.

In addition, the Company has other non-cancelable purchase agreements as of December 31, 2024, under which it is obligated to pay up to an aggregate of $10.7 million to 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, 2024, we had cash and cash equivalents of $411.3 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.

Item 8. Financial Statements and Supplementary Data.

TABLE OF CONTENTS FOR FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Apellis Pharmaceuticals, Inc. and subsidiaries (the "Company") as of December 31, 2024 and 2023, the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity, and cash flows, for each of the three years in the period ended December 31, 2024, 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, 2024 and 2023, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2024, 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, 2024, 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, 2025, expressed an unqualified opinion on the Company's internal control over financial reporting.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our 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.

Inventory Valuation – Refer to Notes 2 and 4 to the financial statements

Critical Audit Matter Description

As described in Note 2 to the consolidated financial statements, inventory is valued at the lower of cost or net realizable value, which requires the Company to eliminate any intercompany profit in inventory. In addition, the Company performs an assessment of the recoverability of capitalized inventory during each reporting period and writes down any excess or obsolete inventories to their estimated realizable value. The determination of whether inventory costs will be realizable requires estimates by management. Provisions for slow-moving, excess or obsolete inventories are made based on the Company's analysis of product dating, inventory levels, historical obsolescence and future sales forecasts.

We identified the valuation of inventory as a critical audit matter due the extent of effort required by the Company to eliminate intercompany profit in inventory and the significant estimates and assumptions used by management to determine excess and obsolescence write downs, including the determination of expected future sales. This required a high degree of auditor judgment and an increased extent of effort when performing audit procedures to evaluate the methodology and the reasonableness of assumptions.

How the Critical Audit Matter Was Addressed in the Audit

Our audit procedures related to valuation of inventory included the following, among others:

- We performed procedures to evaluate the reasonableness and consistency of management's methods used to eliminate intercompany profit, which included testing the accuracy and completeness of underlying data used in management's calculation;
- We independently recalculated the value of inventory to ensure the accuracy and completeness of intercompany profit eliminations;
- We evaluated the Company's estimate for excess and obsolete inventory by performing the following:
    - We evaluated the reasonableness of management's methods, assumptions, and judgments used in developing their estimate, which included consideration of expected future sales, product dating and historical obsolescence experience, and information obtained from the supply chain personnel regarding inventory at risk for excess and obsolescence.
    - We tested the calculation of the excess and obsolete provision pursuant to the Company's policy, on a sample basis, including the accuracy and completeness of the underlying data used in the Company's calculation.
    - We performed a retrospective review by comparing management's prior year estimates of product revenues with actual product revenues in the current year to identify any potential bias.
    - We held discussions with financial and operational management to determine whether any strategic, regulatory, or operational changes in the business were consistent with the projections of future demand that were utilized in estimating the provision recorded.
- We tested the design and effectiveness of controls over inventory valuation, including those over the estimation of provisions for excess and obsolete inventory and controls over the completeness and accuracy of the intercompany profit elimination.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
February 28, 2025

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,	
	2024	2023
Assets		
Current assets:		
Cash and cash equivalents	$ 411,290	$ 351,185
Accounts receivable	264,926	206,442
Inventory	81,404	146,362
Prepaid assets	18,368	38,820
Restricted cash	1,322	1,114
Other current assets	11,644	22,408
Total current assets	788,954	766,331
Non-current assets:		
Right-of-use assets	16,083	16,745
Property and equipment, net	2,952	4,345
Long-term inventory	75,713	—
Other assets	1,349	1,309
Total assets	$ 885,051	$ 788,730
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 38,572	$ 37,516
Accrued expenses	140,184	127,806
Current portion of development liability	—	75,830
Current portion of lease liabilities	6,753	6,441
Total current liabilities	185,509	247,593
Long-term liabilities:		
Long-term development liability	—	239,817
Long-term credit facility	359,489	—
Convertible senior notes	93,341	93,033
Lease liabilities	10,201	11,454
Other liabilities	7,972	2,312
Total liabilities	656,512	594,209
Commitments and contingencies (Note 14)	—	—
Stockholders' equity:		
Preferred stock, $0.0001 par value; 10,000 shares authorized and zero shares issued and outstanding at December 31, 2024 and 2023	—	—
Common stock, $0.0001 par value; 200,000 shares authorized at December 31, 2024 and 2023; 124,495 and 119,556 shares issued and outstanding at December 31, 2024 and 2023, respectively	12	12
Additional paid-in capital	3,267,201	3,035,539
Accumulated other comprehensive loss	(3,308)	(3,542)
Accumulated deficit	(3,035,366)	(2,837,488)
Total stockholders' equity	228,539	194,521
Total liabilities and stockholders' equity	$ 885,051	$ 788,730

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,		
	2024	2023	2022
Revenue:			
Product revenue, net	$ 709,954	$ 366,281	$ 65,092
Licensing and other revenue	71,413	30,310	10,330
Total revenue:	781,367	396,591	75,422
Operating expenses:			
Cost of sales	117,723	58,510	5,636
Research and development	327,570	354,387	387,236
Selling, general and administrative	501,053	500,815	277,163
Total operating expenses:	946,346	913,712	670,035
Net operating loss	(164,979)	(517,121)	(594,613)
Loss on conversion of debt	—	—	(32,890)
Loss on extinguishment of development liability	(1,949)	—	—
Interest income	12,773	20,933	8,914
Interest expense	(40,391)	(29,581)	(32,626)
Other expense, net	(2,170)	(727)	(288)
Net loss before taxes	(196,716)	(526,496)	(651,503)
Income tax expense	1,162	2,132	669
Net loss	$ (197,878)	$ (528,628)	$ (652,172)
Other comprehensive income/(loss):			
Unrealized (loss)/gain on marketable securities	—	—	(1)
Unrealized (loss)/gain on pension plans	591	(2,618)	1,646
Foreign currency translation	(357)	(49)	(430)
Total other comprehensive income/(loss)	234	(2,667)	1,215
Comprehensive loss, net of tax	$ (197,644)	$ (531,295)	$ (650,957)
Net loss per common share, basic and diluted	$ (1.60)	$ (4.45)	$ (6.15)
Weighted-average number of common shares used in net loss per common share, basic and diluted	123,905	118,678	106,114

See accompanying notes to consolidated financial statements

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

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Outstanding Shares	Amount				
Balance at January 1, 2022	97,524	$ 10	$ 1,857,430	$ (2,090)	$ (1,656,688)	$ 198,662
Issuance of common stock in follow-on offering, net of offering costs	8,564	1	380,119	—	—	380,120
Issuance of shares in exchange of Convertible Notes, including issuance costs	3,073	—	129,636	—	—	129,636
Forfeiture of accrued interest in exchange of Convertible Notes		—	1,287	—	—	1,287
Issuance of common stock upon exercise of stock options	1,223	—	21,483	—	—	21,483
Vesting of restricted stock units, net of shares withheld for taxes	252	—	(5,682)	—	—	(5,682)
Share-based compensation expense	—	—	91,085	—	—	91,085
Issuance of common stock to employee stock purchase plan	136	—	4,238	—	—	4,238
Unrealized loss on available-for-sale investments	—	—	—	(1)	—	(1)
Unrealized gain on pension benefit plan	—	—	—	1,646	—	1,646
Net loss	—	—	—	—	(652,172)	(652,172)
Foreign currency translation	—	—	—	(430)	—	(430)
Balance at December 31, 2022	110,772	11	2,479,596	(875)	(2,308,860)	169,872
Issuance of common stock and pre-funded warrants in common stock offering	4,008	1	384,386	—	—	384,387
Issuance of common stock upon exercise of stock options	3,858	—	71,274	—	—	71,274
Vesting of restricted stock units, net of shares withheld for taxes	806	—	(11,040)	—	—	(11,040)
Share-based compensation expense	—	—	105,945	—	—	105,945
Issuance of common stock to employee stock purchase plan	112	—	5,378	—	—	5,378
Unrealized loss on pension benefit plan	—	—	—	(2,618)	—	(2,618)
Net loss	—	—	—	—	(528,628)	(528,628)
Foreign currency translation	—	—	—	(49)	—	(49)
Balance at December 31, 2023	119,556	12	3,035,539	(3,542)	(2,837,488)	194,521
Exercise of pre-funded warrants	2,300	—	—	—	—	—
Proceeds from settlement of capped call	—	—	98,763	—	—	98,763
Issuance of common stock upon exercise of stock options	1,080	—	14,316	—	—	14,316
Vesting of restricted stock units, net of shares withheld for taxes	1,417	—	(57)	—	—	(57)
Share-based compensation expense	—	—	114,128	—	—	114,128
Issuance of common stock to employee stock purchase plan	142	—	4,512	—	—	4,512
Unrealized loss on pension benefit plan	—	—	—	591	—	591
Net loss	—	—	—	—	(197,878)	(197,878)
Foreign currency translation	—	—	—	(357)	—	(357)
Balance at December 31, 2024	124,495	$ 12	$ 3,267,201	$ (3,308)	$ (3,035,366)	$ 228,539

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,		
	2024	**2023**	**2022**
Operating Activities			
Net loss	$ (197,878)	$ (528,628)	$ (652,172)
Adjustments to reconcile net loss to net cash used in operating activities:			
Share-based compensation expense	114,128	105,945	91,085
Loss on conversion of debt	—	—	32,890
Loss on extinguishment of development liability	1,949	—	—
Loss on disposal of fixed assets	—	120	—
Forfeiture of accrued interest in exchange of convertible notes	—	—	1,287
Depreciation expense	1,797	1,784	1,552
Amortization of discounts for credit facility	1,250	—	—
Amortization of discounts for convertible notes	309	297	459
Accretion of discount to development liability	8,936	25,996	26,917
Changes in operating assets and liabilities:			
Accounts receivable	(58,484)	(198,715)	2,375
Inventory	(10,755)	(60,647)	(69,397)
Prepaid assets	20,420	(1,870)	(11,479)
Other current assets	10,793	14,243	32,936
Other assets	705	11,700	17,490
Right-of-use assets and lease liabilities	(277)	(80)	(65)
Accounts payable	1,089	170	18,689
Accrued expenses and other liabilities	18,152	34,950	(6,312)
Net cash used in operating activities	(87,866)	(594,735)	(513,745)
Investing Activities			
Purchase of property and equipment	(403)	(773)	(1,524)
Proceeds from sale of fixed assets	—	99	—
Purchase of available-for-sale securities	—	—	(331,863)
Proceeds from maturity of available-for-sale securities	—	—	393,280
Net cash (used in) provided by investing activities	(403)	(674)	59,893
Financing Activities			
Proceeds from credit facility	365,454	—	—
Payment of issuance cost for credit facility	(7,214)	—	—
Repayment of development liability	(326,533)	—	—
Proceeds from settlement of capped call	98,763	—	—
Proceeds from issuance of common stock, net of issuance costs	—	—	380,120
Proceeds from issuance of common stock, pre-funded warrant offering, net of issuance costs	—	384,387	—
Payments for development liability	—	(55,500)	(34,500)
Proceeds from exercise of stock options	14,316	71,274	21,483
Proceeds from issuance of common stock under employee share purchase plan	4,512	5,378	4,238
Payments of employee tax withholding related to equity-based compensation	(57)	(11,040)	(5,682)
Net cash provided by financing activities	149,241	394,499	365,659
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(659)	135	(488)
Net increase (decrease) in cash, cash equivalents and restricted cash	60,313	(200,775)	(88,681)
Cash, cash equivalents and restricted cash at beginning of period	352,299	553,074	641,755
Cash, cash equivalents and restricted cash at end of period	$ 412,612	$ 352,299	$ 553,074

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,		
	2024	2023	2022
Reconciliation of cash, cash equivalents and restricted cash to the consolidated balance sheets:			
Cash and cash equivalents	$ 411,290	$ 351,185	$ 551,801
Restricted cash	1,322	1,114	1,273
Total cash, cash equivalents, and restricted cash	$ 412,612	$ 352,299	$ 553,074
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 29,368	$ 3,286	$ 5,003
Cash paid for income taxes	$ 1,649	$ —	$ 4,915
Proceeds from income tax refunds net of income taxes paid	$ —	$ 1,759	$ —
Convertible Notes exchanged for common stock	$ —	$ —	$ 98,086

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 included organizing and staffing the Company, acquiring rights to product candidates, business planning, raising capital, developing its product candidates, commercializing EMPAVELI (pegcetacoplan) for the treatment of paroxysmal nocturnal hemoglobinuria ("PNH") and commercializing SYFOVRE (pegcetacoplan injection) for the treatment of geographic atrophy secondary to age-related macular degeneration ("GA").

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").

Follow-on Public Offerings

On February 22, 2023, the Company issued and sold 4,007,936 shares of common stock and, in lieu of common stock to investor who so chose, pre-funded warrants to purchase 2,380,956 shares of common stock in a follow-on offering, including 833,333 shares sold pursuant to the underwriters' exercise in full of their option to purchase additional shares of common stock. The price to the public of the shares of common stock was $63.00 per share and the price to the public of the pre-funded warrants was $62.9999 per pre-funded warrant. The pre-funded warrants have an exercise price equal to $0.0001 per share and do not expire. The pre-funded warrants were accounted for as equity instruments. The Company received total net proceeds of $384.4 million, after deducting underwriting discounts and commissions of $18.8 million and offering costs of $0.3 million. For the period ended December 31, 2024, 2,299,991 shares of common stock were issued from the exercise of pre-funded warrants. As of December 31, 2024, the Company has pre-funded warrants to purchase 80,956 shares of our common stock outstanding.

On March 28, 2022, the Company issued and sold 8,563,830 shares of its common stock at a price per share to the public of $47.00 in a follow-on public offering including an additional 1,117,021 shares of its common stock that were sold at the follow-on public offering price of $47.00 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 $380.1 million after deducting underwriting discounts and commissions of approximately $22.1 million and offering costs of $0.3 million for these transactions.

Liquidity and Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. From inception to December 31, 2024, the Company has incurred cash outflows from operations, losses from operations, and had an accumulated deficit of $3.0 billion, primarily as a result of expenses incurred through a combination of research and development activities related to the Company's various product candidates and expenses supporting those activities and expenses incurred in connection with product launches and commercialization costs.

The Company believes that its cash and cash equivalents of $411.3 million at December 31, 2024 combined with cash anticipated to be generated from sales of EMPAVELI and from SYFOVRE will be sufficient to fund its operations and capital expenditure requirements for at least twelve months from the date of issuance of these consolidated financial statements.

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. 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 ("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 SYFOVRE and revenue derived from its collaboration arrangement with Sobi. See Note 11, 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 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

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 and SYFOVRE in February 2023. The Company sells EMPAVELI and SYFOVRE 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. 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 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:

Fees

Distribution Fees: Distribution fees include distribution service fees paid to SDs based on a contractually fixed percentage of the wholesale acquisition cost (WAC). These fees are directly related to the storage, handling and distribution of product to customers, and are therefore inseparable from the product. Distribution fees are recorded as an offset to revenue based on contractual terms at the time revenue from the sale is recognized.

Credit Card Fees: SDs will sell downstream to customers who may pay for product via credit card. The Company will reimburse its SDs for the credit card fees incurred as a result of SDs accepting credit cards as a form of payment from the downstream customers. Credit card fees are recorded as an offset to revenue based on the average aggregate credit card rate as a percentage of SD sales at the time revenue from the sale is recognized.

Patient Assistance

Copay: Other incentives include voluntary patient assistance programs, such as the Company's co-pay assistance program, which are intended to provide financial assistance to qualified commercially-insured patients with prescription drug co-payments required by

payors. The adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability.

The Company also estimates the number of patients in the prescription drug coverage gap for whom the Company will owe an additional liability under the Medicare Part D program.

Rebates

Government Rebates: The Company's products are subject to pricing limits under certain federal government programs. Qualifying entities (i.e., end-users) purchase products from the Company's customers at their qualifying discounted price. The chargeback amount the Company incurs represents the difference between the Company's contractual sales price to the customer, and the end-user's applicable discounted purchase price under the government program.

Other Rebates: The Company contracts with certain payor organizations, primarily group purchasing organizations ("GPOs") and pharmacy benefit managers, for the payment of rebates with respect to utilization of the Company's products. The Company estimates these rebates and records such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability.

Group purchasing organizations 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 the GPOs. The Company issues credit notes for the chargeback which are applied to future sales.

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) and the underlying product demand.

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 the 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. The Company assesses 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.

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 in deciding how to allocate resources and in assessing performance. The Company's chief operating decision maker ("CODM") is the chief executive officer ("CEO"). The Company manages its operations as a single operating segment. See Note 17, Segment Information, for additional information.

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: accrued research and development expenses, reserves for variable consideration and reserves for excess or obsolete inventories.

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, and Note 10, 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.

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 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 as of December 31, 2024 and 2023, and its payment terms are generally 30-65 days for EMPAVELI and 60-150 days for SYFOVRE. 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, 2024 and December 31, 2023, 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.

The Company has an agreement (the "Factoring Agreement") to sell certain trade accounts receivable to a third-party financial institution at a discount to the invoiced amount. Under the Factoring Agreement, the maximum amount of outstanding accounts receivables sold at any time is $100.0 million. The Company accounts for the transfer of trade accounts receivable under the Factoring Agreement as a sale in accordance with ASC 860, *Transfers and Servicing*, because effective control and risk associated with the transferred accounts receivable is passed to the third-party. Accordingly, the Company derecognizes the sold trade accounts receivable from the consolidated balance sheets. Cash proceeds related to the accounts receivable sold are included in cash from operating activities in the consolidated statements of cash flows. Any discounts or fees incurred in connection with the sales are recorded within "Selling, general and administrative expenses" in the consolidated statements of operations and comprehensive loss. Pursuant to the Factoring Agreement, the Company performs certain collection and administrative functions for the receivable sold. The fair value of these administrative services is not material and therefore, the Company has not recorded any servicing assets or liabilities associated with the Factoring Agreement. See Note 3, Product Revenues, Accounts Receivable, and Reserves for Product Sales, for additional 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, labor, overhead and freight. The Company performs an assessment of the recoverability of inventory during each reporting period, and it writes down any excess and obsolete inventories to their estimated realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, are recorded within cost of sales. The determination of whether inventory costs will be realizable requires estimates by management. Provisions for potentially obsolete or slow-moving inventory, are made based on the Company's analysis of product dating, inventory levels, historical obsolescence and future sales forecasts. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required which would be recorded as a cost of sales in the consolidated statements of operations and comprehensive loss.

Inventory not expected to be sold within the Company's normal operating cycle is classified as long-term inventory on the consolidated balance sheet.

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 its 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. Inventory that can be used in either the production of clinical or commercial product is expensed as research and development expense when selected for use in a clinical manufacturing campaign.

Shipping and handling costs for product shipments are recorded as incurred in cost of sales along with costs associated with manufacturing the product and any inventory write-downs.

Foreign Currency

The functional currency of each of the Company's subsidiaries is its local currency, except for the wholly owned subsidiaries Apellis Europe B.V. and Apellis International GmbH where the functional currency is the U.S. dollar. 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.

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.

Selling, General and Administrative

Costs incurred in connection with selling, general and administrative activities are expensed as incurred. Selling, general and administrative expenses consist primarily of employee-related expenses including salaries, bonuses, benefits and share-based compensation, consulting and professional fees, marketing and advertising costs, medical affairs and regulatory costs associated with our commercial products, 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. Marketing and advertising costs include marketing literature, promotional activities, conferences and seminars, branding and sponsorships.

For the years ended December 31, 2024, 2023 and 2022, the Company incurred advertising costs of $83.3 million, $86.5 million, and $56.5 million, respectively.

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 basis 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 using a more likely than not threshold for recognizing and resolving uncertain tax positions. 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, 2024 and 2023, the Company did not have any significant uncertain tax positions

Share-Based Compensation

The Company's stock-based compensation program allows for grants of stock options and restricted stock units.

The Company measures stock-based compensation cost at the grant date based on the fair value of the option and restricted stock units and recognizes the expense related to awards on a straight-line basis over the requisite service period of the option, which is typically the vesting period. Forfeitures are recognized as they occur.

The Company estimates the fair value of each option using the Black-Scholes option pricing model that considers the fair value of its common stock, the exercise price, the expected life of the option, the expected volatility of its common stock, expected dividends on its common stock, and the risk-free interest rate over the expected life of the option. The Company uses the simplified method described in the SEC's Staff Accounting Bulletin No. 107, Share-Based Payment, to determine the expected life of the option grants. The estimate of expected volatility is based on the Company's historical volatility over a period commensurate with the option's expected term. The Company has never declared or paid any cash dividends on its common stock and does not expect to do so in the foreseeable future. Accordingly, it uses an expected dividend yield of zero. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant valuation for a period commensurate with the option's expected term.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk include cash and cash equivalents and accounts receivable.

The Company is exposed to credit risk in the event of default by the financial institutions holding its cash and the issuers of its cash equivalents. The Company maintains its cash and cash equivalents with highly-rated, federally-insured financial institutions. At times, such amounts may exceed federally-insured limits. 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.

Billings to large specialty pharmacies and specialty distributors account for the majority of the Company's accounts receivables, and collateral is generally not required from these customers. To mitigate credit risk, the Company monitors the financial performance and credit-worthiness of its customers. See Note 3, Product Revenues, Accounts Receivable, and Reserves for Product Sales for additional information.

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. The issuance of common stock in connection with the pre-funded warrants are included in weighted-average shares outstanding and therefore, are included in the calculation of basic net loss per common share. For purposes of the diluted net loss per share calculation, convertible notes, common stock options and restricted stock 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.

Recent Accounting Pronouncements issued not yet adopted

In November 2024, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update (ASU) 2024-03, Income Statement - Reporting Comprehensive Income - Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses, which requires additional disclosure of the nature of expenses included in the income statement. The standard requires disclosures about specific types of expenses included in the expense captions presented in the income. This ASU is effective for fiscal years beginning after December 15, 2026, and interim periods beginning after December 15, 2027, with early adoption permitted. The requirements should be applied on a prospective basis while retrospective application is permitted. We are currently evaluating the impact that the adoption of this guidance will have on our disclosures.

In December 2023, the FASB issued ASU 2023-09, Improvements to Income Tax Disclosures. This standard is an amendment to the accounting guidance on income taxes which requires entities to provide additional information in the rate reconciliation and additional disaggregated disclosures about income taxes paid. This guidance requires public entities to disclose in their rate reconciliation table additional categories of information about federal, state, and foreign income taxes and to provide more details about the reconciling items in some categories if the items meet a quantitative threshold. The guidance is effective for annual periods beginning after December 15, 2024. We are currently evaluating the impact that the adoption of this guidance will have on our disclosures.

Recently adopted accounting pronouncements

In November 2023, the FASB issued an amendment to the accounting guidance on segment reporting. The amendments require disclosure of significant segment expenses and other segment items and requires entities to provide in interim periods all disclosures about a reportable segment's profit or loss and assets that are currently required annually. The amendment also requires disclosure of the title and position of the chief operating decision maker ("CODM") and an explanation of how the CODM uses the reported measure(s) of segment profit or loss in assessing segment performance and deciding how to allocate resources. The guidance is effective for fiscal years beginning after December 15, 2023, and interim periods within fiscal years beginning after December 15, 2024. Retrospective application is required, and early adoption is permitted. The Company adopted the accounting guidance on segment reporting during the year ended December 31, 2024. See Note 17 Segment Information in the accompanying notes to the consolidated financial statements for further detail.

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 and approval for the sale of SYFOVRE in the United States in February 2023. The Company's product revenues, net of sales discounts and allowances and reserves as of December 31, 2024, 2023 and 2022 totaled $710.0 million, $366.3 million and $65.1 million. The Company's product revenues consist of sales of EMPAVELI and SYFOVRE to specialty pharmacies and specialty distributors.

The table reflects net product revenue by major source for the following periods (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Products:			
EMPAVELI	$ 98,091	$ 91,033	$ 65,092
SYFOVRE	611,863	275,248	—
Total product revenue, net	$ 709,954	$ 366,281	$ 65,092

The Company's accounts receivable balance of $264.9 million as of December 31, 2024 and $206.4 million as of December 31, 2023 primarily consisted of EMPAVELI and SYFOVRE product sales receivable and licensing and other revenue receivables from its collaboration with Sobi. The Company does not have a reserve related to expected credit losses against its accounts receivable balance and expects to collect its accounts receivable in the ordinary course of business.

The Company's product sales reserves totaled $45.1 million and $16.6 million as of December 31, 2024 and 2023. respectively. These amounts are included in accrued expenses on the Company's consolidated balance sheet as of December 31, 2024.

The following table summarizes activity in each of the product revenue allowance and reserve categories as of December 31, 2024 (in thousands):

	Fees and patient assistance	Government and other rebates	Returns	Total
Ending balance at December 31, 2022	$ 164	$ 1,936	$ 251	$ 2,351
Provision related to sales in the current year	17,690	26,661	4,698	49,050
Adjustments related to prior period sales	(112)	(1,223)	(2,481)	(3,817)
Credits and payments made	(12,068)	(18,476)	(415)	(30,960)
Ending balance at December 31, 2023	$ 5,674	$ 8,898	$ 2,053	$ 16,625
Provision related to sales in the current year	46,506	89,094	3,936	139,536
Adjustments related to prior period sales	1,461	(19)	(96)	1,346
Credits and payments made	(42,052)	(66,440)	(3,870)	(112,362)
Ending balance at December 31, 2024	$ 11,589	$ 31,533	$ 2,023	$ 45,145

Significant customers - Gross product revenues and product sales receivable from the Company's customers who individually accounted for 10% of more of total gross product revenues and/or 10% or more of total product sales receivable consisted of the following:

	Percent of Total Gross Product Revenues Year Ended December 31,		
	2024	2023	2022
Customer A	13%	24%	99%
Customer C	19%	16%	—
Customer D	59%	54%	1%

	Percent of Product Sales Receivable As of December 31,	
	2024	2023
Customer A	3%	4%
Customer C	29%	22%
Customer D	55%	66%

Factoring of accounts receivable and associated fees for the years ended December 31, 2024 and 2023 were as follows (in thousands):

	December 31, 2024	December 31, 2023	December 31, 2022
Accounts receivable sold	$ 142,698	$ —	$ —
Less: factoring fees	(1,700)	—	—
Net cash proceeds	$ 140,998	$ —	$ —

The accounts receivable sold that remained outstanding as of December 31, 2024 and 2023 was $86.1 million and zero, respectively.

4. Inventory

The Company's inventory of EMPAVELI and SYFOVRE consisted of the following as of December 31, 2024 and 2023 (in thousands):

	December 31, 2024	2023
Raw materials	$ 54,385	$ 32,724
Semi-finished goods	92,872	82,924
Finished goods	9,860	30,714
Total inventories	$ 157,117	$ 146,362

The Company's long-term inventory balance consists of raw materials and semi-finished goods that are not expected to be sold within the Company's normal operating cycle.

Inventory amounts written down as a result of excess, obsolete, unmarketability or other reasons are charged to cost of sales. For the years ended December 31, 2024 and 2023, the Company recognized write-downs of $19.0 million and $6.4 million, respectively.

5. Prepaid and Other Current Assets

Prepaid assets and other current assets consisted of the following as of December 31, 2024, and 2023 (in thousands):

	December 31, 2024	2023
Down payments for inventory	$ 1,080	$ 16,296
Prepaid research and development	7,780	13,931
Other prepaid assets	9,508	8,593
Total prepaid assets	$ 18,368	$ 38,820

	December 31, 2024	2023
Royalties receivable	$ 4,525	$ 3,054
Receivable from collaboration agreement (1)	2,272	15,000
Deposits and other current assets	4,847	4,354
Total other current assets	$ 11,644	$ 22,408

(1) In January 2024 the Company waived the remaining reimbursement payment of $15.0 million in connection with the decision to discontinue the cold agglutinin disease ("CAD") program. As the reimbursement was related to development costs under the Sobi collaboration agreement, this amount was recorded to research and development expense in the consolidated statements of operations for the period ended December 31, 2024.

6. Development Liability

In 2019, the Company entered into a development funding agreement (as amended, the "SFJ agreement") with SFJ Pharmaceuticals Group ("SFJ"), under which SFJ agreed to provide funding to the Company to support the development of pegcetacoplan for the treatment of patients with PNH. Under the SFJ agreement, SFJ paid the Company an aggregate of $140.0 million between June 2019 and January 2020.

Under the SFJ agreement, 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.

Following regulatory approval for the use of systemic pegcetacoplan as a treatment for PNH by the FDA in May 2021 and by the European Medicines Agency in December 2021, the Company became obligated to pay SFJ an aggregate of $460.0 million in payments over the period from the time of each regulatory approval until the sixth anniversary of each regulatory approval. The Company paid SFJ a total of $94.0 million through March 31, 2024.

From December 15, 2021 to the final annual payment due in December 2027, the development liability was accreted from its initial carrying amount to the total payment amount using the effective interest rate method over the remaining life of the SFJ agreement. The difference between the carrying amount and the total payment amount is presented as a discount to the development liability. The accretion is recorded as interest expense in the consolidated statement of operations and comprehensive loss.

In May 2024, the Company paid its remaining obligations under the SFJ agreement in full with $326.5 million of proceeds from the Sixth Street Financing Agreement (as defined below) (see Note 8). Upon such payment, SFJ released its security interest in the Company's assets at that time. The Company concluded that the development liability was extinguished as of the payoff date, and the difference of $1.9 million between the reacquisition price of $326.5 million and the net carrying value of the development liability of $324.6 million was recorded as a loss on the extinguishment of the development liability in the consolidated statement of operations and comprehensive loss for the period ended December 31, 2024.

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

	December 31,		Effective Interest Rate
	2024	2023	
Development liability	$ —	$ 366,000	7.91%
Less: Unamortized discount to development liability	—	(50,353)	
Less: Current portion of development liability, net of discount	—	(75,830)	
Total long term development liability	$ —	$ 239,817	

For the years ended December 31, 2024, 2023 and 2022 interest expense of $8.9 million, $26.0 million and $26.9 million, respectively was recorded for the accretion of the development liability.

7. Accrued Expenses

Accrued expenses consisted of the following as of December 31, 2024 and 2023 (in thousands):

	December 31,	
	2024	2023
Accrued research and development	$ 22,782	$ 28,318
Accrued royalties	7,147	10,197
Accrued payroll liabilities	40,888	51,781
Product revenue reserves	45,145	16,625
Commercial costs	20,610	8,715
Other	3,612	12,170
Total accrued expenses	$ 140,184	$ 127,806

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 2019 Convertible Notes and the 2020 Convertible Notes are referred to together as the Convertible Notes. 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 their terms.

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.

The conditional conversion feature of the Convertible Notes was not triggered as of December 31, 2024.

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.

After September 20, 2023, the Company may redeem for cash all or a portion of the Convertible Notes, at its option, 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 calls any Convertible Notes for redemption, it will constitute a "make-whole fundamental change" with respect to such Convertible Notes, in which case the conversion rate applicable to the conversion of such Notes, if converted in connection with the redemption, will be

increased in certain circumstances. The Company has not called for redemption or redeemed any of the Convertible Notes as of December 31, 2024.

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.

In January 2021, July 2021 and July 2022, the Company entered into separate, privately negotiated exchange agreements to modify the conversion terms with certain holders of its 2019 Convertible Notes and 2020 Convertible Notes. Under the terms of these exchange agreements, in January 2021, July 2021 and July 2022, the holders exchanged approximately $126.1 million of 2019 Convertible Notes, $201.1 million of 2019 Convertible Notes, and $98.1 million of 2020 Convertible Notes, respectively, in aggregate principal amount held by them for an aggregate of 3,906,869 shares, 5,992,217 shares and 3,027,018 shares, respectively, of common stock issued by the Company. 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, which resulted in the expensing of the fair value of the shares that were issued in excess of the original terms of the Convertible Notes.

As of December 31, 2024 and 2023, the Company held in treasury Convertible Notes in principal amount of $425.4 million which have not been cancelled.

The outstanding balance of the Convertible Notes as of December 31, 2024 and 2023 consisted of the following (in thousands):

	December 31,	
	2024	2023
Principal	93,897	93,897
Less: debt discount and issuance costs, net	$ (556)	$ (864)
Net carrying amount	93,341	93,033

The following table sets forth total interest expense recognized related to the Convertible Notes during the years ended December 31, 2024, 2023 and 2022 (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Amortization of debt issuance costs	309	297	459
Contractual interest expense	3,286	3,286	5,248
Total interest expense	$ 3,595	$ 3,583	$ 5,707

Capped Call Transactions

On September 11, 2019 and May 6, 2020, concurrently with the pricings of the Convertible Notes, the Company entered into capped call transactions with two counterparties. The capped call transactions are expected generally to reduce the potential dilution to the Company's common stock upon any conversion of Convertible Notes and/or offset any cash payments the Company is required to make in excess of the principal amount of converted Convertible Notes, as the case may be, in the event that the market price per share of the Company's common stock, as measured under the terms of the capped call transactions, is greater than the strike price of the capped call transactions, which is initially $39.4625 (the conversion price of the Convertible Notes) and is subject to anti-dilution adjustments substantially similar to those applicable to the conversion rate of such Convertible Notes. If, however, the market price per share of the Company's common stock, as measured under the terms of the capped call transactions, exceeds the cap price of the capped call transactions, which is initially $63.14 per share, 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.

On February 27, 2024, the Company unwound a portion of the capped call transactions with the capped call counterparties, which resulted in cash proceeds to the Company of $98.8 million. The unwind transactions were settled at a volume-weighted average price per share of $64.11 on March 8, 2024.

As of December 31, 2024, the Company holds remaining capped call transactions in a notional amount corresponding to $93.9 million principal amount of Convertible Notes.

Financing Agreement and Credit Facility

On May 13, 2024, the Company and certain of its subsidiaries entered into a financing agreement (the "Sixth Street Financing Agreement") with the lenders party thereto (the "Lenders"), and Sixth Street Lending Partners ("Sixth Street"), as the administrative agent and collateral agent for the Lenders.

The Sixth Street Financing Agreement provides for a senior secured term loan facility of up to $475.0 million (the "Credit Facility"), consisting of an initial draw of $375.0 million at closing and a potential additional $100.0 million draw at the Company's option upon satisfaction of a $50.0 million minimum cash requirement and a requirement that the Company's trailing three-month sales of SYFOVRE is at least $180.0 million prior to the $100.0 million draw. The Company can exercise the option for the $100.0 million draw through September 30, 2025, assuming such requirements are met.

The Credit Facility matures on May 13, 2030 (the "Maturity Date") and bears interest at (i) in the case of SOFR Loans, an annual rate equal to 3-month Term SOFR (subject to 1.00% floor), plus 5.75%, and (ii) in the case of Base Rate Loans, an annual rate equal to the base rate as defined in the agreement (subject to 2.00% floor), plus 4.75%. Certain additional commitment and undrawn amount fees are also payable in connection with the Credit Facility.

The net proceeds from the initial draw of the Credit Facility were approximately $358.2 million, net of $16.8 million of issuance costs. The Company used $326.5 million of the proceeds from the initial draw of the Credit Facility to buy out its remaining obligations to SFJ. The buyout of the SFJ development liability eliminated $366.0 million in payments to SFJ between 2024 and 2027, including approximately $200.0 million payable through 2025 (See Note 6).

The Credit Facility does not provide for scheduled amortization payments during the term. All principal will be due on the Maturity Date. The Company will have the right to prepay loans under the Credit Facility at any time. The Company is required to repay loans under the Credit Facility with proceeds from certain asset sales, condemnation events and extraordinary receipts, subject, in some cases, to reinvestment rights. Repayments are subject to a prepayment premium. Repayments may be made after the first year of the loan and are subject to a prepayment premium up to 3% depending on timing.

All obligations under the Sixth Street Financing Agreement are secured on a first-priority basis, subject to certain exceptions, by security interests in substantially all assets of the Company and certain subsidiaries of the Company, including its intellectual property, and are guaranteed by certain subsidiaries of the Company, including foreign subsidiaries, subject to certain exceptions.

The Sixth Street Financing Agreement contains customary covenants, including, without limitation, a financial covenant to maintain liquidity of at least $50.0 million if the Company's market capitalization is below $3.0 billion, and negative covenants that, subject to certain exceptions, restrict indebtedness, liens, investments (including acquisitions), fundamental changes, asset sales and licensing transactions, dividends, modifications to material agreements, payment of subordinated indebtedness, and other matters customarily restricted in such agreements. Among other permissions, the Company is permitted, on terms and conditions set forth on the Sixth Street Financing Agreement, to enter into a separate asset-based financing arrangement with a third party in an amount of up to $100.0 million, which amount is increased to $200.0 million upon certain sales or market capitalization thresholds, and to have outstanding convertible unsecured notes in an amount equal to the greater of $400.0 million and 10% of the Company's market capitalization, but not to exceed $600.0 million. The Company is subject to restrictions on sales and licensing transactions with respect to its core intellectual property, defined to include SYFOVRE, EMPAVELI, and other pegcetacoplan product assets, subject to certain exceptions, including certain transactions related to areas outside the United States and Europe.

The outstanding balance of the Credit Facility as of December 31, 2024 and 2023 consisted of the following (in thousands):

	December 31, 2024	December 31, 2023
Principal	$ 375,000	$ —
Less: debt discount and issuance costs	(15,511)	—
Net carrying amount	$ 359,489	$ —

The following table sets forth total interest expense recognized related to the Credit Facility as of December 31, 2024 and 2023 (in thousands):

	December 31, 2024	December 31, 2023
Amortization of debt issuance costs	$ 1,250	$ —
Contractual interest expense	26,082	—
Total interest expense	$ 27,332	$ —

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 of December 31, 2024 and 2023, all leases were classified as operating leases. Additional information related to the operating leases is as follows (in thousands):

	December 31, 2024	December 31, 2023
Right-of-use assets	$ 16,083	$ 16,745
Operating lease liabilities	$ 16,954	$ 17,895
Weighted average remaining term in years	2.73	2.83
Weighted average discount rate used to measure outstanding lease liabilities	6.20%	7.20%

For the years ended December 31, 2024, 2023, and 2022, the total lease cost for operating leases was approximately $10.2 million, $7.0 million, and $6.2 million, respectively.

Supplemental cash flow information related to operating leases for the years ended December 31, 2024, 2023 and 2022 is as follows (in thousands):

	2024	2023	2022
Operating cash flows from operating leases	$ 9,263	$ 7,939	$ 7,375
Operating lease assets obtained in exchange for lease obligations	—	2,700	—

The maturity of the Company's operating lease liabilities as of December 31, 2024 are as follows (in thousands):

2025	$ 7,468
2026	7,076
2027	2,351
2028	559
2029 and thereafter	853
Total future minimum lease payments	18,307
Less imputed interest	(1,353)
Total operating lease liabilities	$ 16,954

10. Fair Value Measurements

The following table presents the fair value of the Company's financial instruments that are measured at fair value measurement on a recurring basis as of December 31, 2024 and 2023 (in thousands):

Balance Sheet Classification: Type of Instrument	December 31, 2024			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Cash and cash equivalents: Money market funds	$ 276,868	$ —	$ —	$ 276,868
Total Financial Assets	$ 276,868	$ —	$ —	$ 276,868

Balance Sheet Classification: Type of Instrument	December 31, 2023			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Cash and cash equivalents: Money market funds	$ 276,391	$ —	$ —	$ 276,391
Total Financial Assets	$ 276,391	$ —	$ —	$ 276,391

The Company's Convertible Notes and development liability are financial instruments that are reported in the consolidated financial statements at historical cost. The Convertible Notes are Level 1 within the fair value level hierarchy as of December 31, 2024 and 2023. The fair value of the Convertible Notes was $102.3 million as of December 31, 2024 and $140.8 million as of December 31, 2023. 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 as of December 31, 2024 and 2023.

The fair value of the development liability was $306.9 million as of December 31, 2023. The development liability is Level 2 within the fair value hierarchy based on the discounting of fixed cash flows using an observed bond yield for borrowers with similar credit rating.

11. License and Collaboration Agreements

Sobi License and Collaboration Agreement

In October 2020, the Company and its subsidiaries, Apellis Switzerland GmbH and APL DEL Holdings, LLC, entered into a Collaboration and License Agreement (the "Sobi 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").

Under the Sobi 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 Sobi collaboration agreement, the Company and Sobi agreed to collaborate to develop Licensed Products for certain indications, including PNH, C3G, IC-MPGN and HSCT-TMA (collectively the "Initial Indications"), 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 PNH in the European Union and the United Kingdom. The Company and Sobi formed 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. The Sobi 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. For the period ended December 31, 2024 and 2023, the Company

recognized revenue of $53.0 million and $15.3 million, respectively, for the supply of Licensed Products to Sobi, which is included in License and other revenue on the consolidated statements of operations and comprehensive loss income.

Sobi paid the Company 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, of which the Company received $50.0 million in April 2022 for the achievement of a regulatory development milestone in Europe. Sobi also agreed to reimburse the Company for up to $80.0 million in development costs, of which the Company received a total of $65.0 million through January 2023 and waived the remaining payment of $15.0 million in January, 2024. 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 Sobi collaboration agreement, the Company remains responsible for its license fee obligations (including royalty obligations) to the Trustees of the University of Pennsylvania ("Penn"), as a licensor of the Company.

Under the Sobi collaboration agreement, as of December 31, 2024, 2023 and 2022, the Company recognized $18.4 million, $10.0 million and $3.0 million, respectively, of royalty revenue from sales of Aspaveli, which was sold by Sobi outside of the United States.

As of December 31, 2024, the Company did not recognize any contra-research and development expense in the consolidated statement of operations and comprehensive loss related to the $80.0 million reimbursement commitment from Sobi. Since contract inception, the Company has recognized $65.0 million in contra-research and development expenses and waived the remaining $15.0 million in connection with the decision to discontinue the CAD program.

As of December 31, 2023, the Company recorded $15.0 million in other current assets, which represented the receivable for contra-research and development expenses incurred but not yet reimbursed from Sobi. In January 2024, the Company waived the remaining reimbursement payment of $15.0 million in connection with the decision to discontinue the CAD program.

University of Pennsylvania License Agreement

The Company is a party to a license agreement with Penn for an exclusive, worldwide license to specified patent rights. The Company is 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, subject to a step-down upon patent expiry, with minimum quarterly royalty thresholds. In addition, the Company is obligated to pay a specified portion of income it receives from sublicensees.

In April 2023, the Company paid $2.3 million for the achievement of a regulatory milestone as a result of the FDA approval of SYFOVRE in February 2023. In 2023, the Company incurred $5.0 million as a result of the achievement of sales milestones for SYFOVRE of which the Company paid $2.0 million in October 2023 and the remaining $3.0 million in January 2024.

As of December 31, 2024 and 2023 respectively, the Company has incurred royalty expense of $19.8 million and $8.9 million on sales of SYFOVRE, which is included in cost of sales on the consolidated statements of operations and comprehensive loss income.

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 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 a step-down upon patent expiry, with 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 a sublicense fee owed to Penn related to the Sobi collaboration agreement and another licensing transaction. In August 2021, the Company paid $1.0 million to Penn upon the achievement of a development milestone, net of a credit for the annual license maintenance payment. In June 2022, the Company paid an additional $5.0 million to Penn upon the achievement of a development milestone. In January 2023, the Company paid $1.0 million to Penn upon the achievement of a sales milestone for EMPAVELI in 2022. In January 2024, the Company paid $0.5 million for a sublicense fee owed to Penn related to Sobi obtaining regulatory approval in Japan. Additionally, in January 2024, the Company paid $1.5 million as a result of the achievement of a sales milestone for EMPAVELI and Aspaveli.

As of December 31, 2024, 2023 and 2022, the Company has incurred royalty expense of $6.4 million, $4.8 million and $2.7 million, respectively, on sales of EMPAVELI and Aspaveli, which is included in cost of sales on the consolidated statements of operations and comprehensive loss.

Beam Research Collaboration

In June 2021, the Company entered into an exclusive five-year research collaboration (the "Beam collaboration agreement") with Beam Therapeutics, Inc. ("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 Beam collaboration agreement, the Company 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 Beam 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 Beam collaboration agreement and upon such election any license agreement in place at that time, would be terminated.

As part of the Beam collaboration agreement, 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 paid an additional $25.0 million on the first anniversary of the Beam collaboration agreement in June 2022. The Company and Beam are each 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 Beam collaboration agreement 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 Beam 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 FASB ASC Topic 730, Research and Development ("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.

12. Employee Retirement Plans

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 2024, 2023 and 2022, the Company recorded $5.1 million, $5.7 million, and $4.3 million respectively, for employer contributions made to the 401(k) Plan.

The Company maintains a pension plan covering employees of its Swiss subsidiary, Apellis International GmbH (f/k/a Apellis Switzerland GmbH) (the "Swiss Plan"). The Swiss Plan is a government-mandated retirement fund that provides employees with a minimum benefit. Employer and employee contributions are made to the Swiss Plan based on various percentages of salary and wages that vary according to employee age and other factors. As is customary with Swiss pension plans, the assets of the Swiss Plan are invested in a collective fund, which are held and invested by a Swiss insurance company. The investment strategy of the Swiss Plan is managed by an independent asset manager with the objective of achieving a consistent long-term return which will provide sufficient funding for future pension obligations while limiting risk.

As of December 31, 2024, the Swiss Plan was underfunded by $1.6 million as the fair value of the plan assets of $16.7 million was less than the projected benefit obligation of $18.3 million. The accumulated benefit obligation at December 31, 2024 was $0.6 million. The Company's net periodic benefit cost for the year ended December 31, 2024 was $1.2 million. The contributions to the Swiss Plan for the year ended December 31, 2024 were not material.

As of December 31, 2023, the Swiss Plan was underfunded by $2.2 million as the fair value of the plan assets of $16.2 million was less than the projected benefit obligation of $18.4 million. The accumulated benefit obligation at December 31, 2023 was $2.6 million. The Company's net periodic benefit cost for the year ended December 31, 2023 was $0.9 million. The contributions to the Swiss Plan for the year ended December 31, 2023 were not material.

13. Income Taxes

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

	Year Ended December 31,		
	2024	2023	2022
United States	$ (22,701)	$ (48,495)	$ (82,815)
Foreign	(174,015)	(478,001)	(568,688)
Total	$ (196,716)	$ (526,496)	$ (651,503)

Provision for income taxes for the years ended December 31, 2024, 2023, and 2022 are as follows (in thousands):

	Year Ended December 31, 2024	Year Ended December 31, 2023	Year Ended December 31, 2022
Current income tax expense:			
U.S. Federal	$ —	$ —	$ —
U.S. State and Local	474	1,869	520
Foreign	688	263	149
Total current income tax expense	1,162	2,132	669
Deferred income tax expense:			
U.S. Federal	—	—	—
U.S. State and Local	—	—	—
Foreign	—	—	—
Total deferred income tax expense	—	—	—
Total tax expense	$ 1,162	$ 2,132	$ 669

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

	Year Ended December					
	2024		2023		2022	
	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	$ (41,310)	21.0%	$(110,564)	21.0%	$(136,816)	21.0%
Foreign tax rate differential	16,791	(8.5)	42,100	(8.0)	50,219	(7.7)
State income taxes, net of federal benefit	(18,218)	9.3	(13,438)	2.6	9,051	(1.4)
Change in valuation allowances	11,106	(5.6)	119,592	(23.2)	94,668	(14.5)
Tax credits	(22,100)	11.2	(11,566)	2.2	(19,966)	3.0
GILTI Inclusion Income	59,627	(30.3)	—	—	—	—
Share Based Compensation	(8,688)	4.4	(26,881)	5.1	—	—
Change in state apportionment	—	—	—	—	(35)	—
Loss on debt conversion	—	—	—	—	6,626	(1.0)
Permanent and other	3,954	(2.1)	2,889	(0.1)	(3,078)	0.5
Effective income tax provision	$ 1,162	(0.6)	$ 2,132	(0.4)	$ 669	(0.1)

The Company's effective income tax rate for the year ended December 31, 2024 compared to the year ended December 31, 2023 increased primarily as a result of operations in state jurisdictions.

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

	December 31,	
	2024	2023
Deferred tax assets:		
Intangible assets	$ 177,244	$ 160,281
Research and development capitalization	21,474	32,163
Share-based compensation	38,494	31,712
Net operating loss carryforwards	312,672	329,135
Research and development credits	81,340	67,667
Orphan drug credits	48,015	34,023
Development derivative liability	—	75,190
Convertible debt	1,021	5,582
Fixed Assets	194	18
Lease liability	3,026	2,888
Accruals	7,668	9,998
Deferred Interest Expense	1,974	—
Inventory Reserves	31,476	6,317
UNICAP	1,806	1,086
Total deferred tax assets	726,404	756,060
Deferred tax liabilities:		
Fixed assets	—	—
Right-of-use asset	(2,821)	(2,672)
Total deferred tax liabilities	(2,821)	(2,672)
Net deferred tax assets before allowance:	723,583	753,388
Less valuation allowance	(723,583)	(753,388)
Net deferred tax assets	$ —	$ —

Management has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets and has determined that it is more likely than not that the Company will not recognize the benefits of its net federal, foreign and state deferred tax assets, and as a result, a valuation allowance of $723.6 million and $753.4 million has been established at December 31, 2024 and 2023, respectively. The decrease in the valuation allowance of $29.8 million was primarily driven by the utilization of federal and foreign net operating losses and pay-down of the development liability with SFJ.

The Tax Cuts and Jobs Act (TCJA) requires taxpayers to capitalize and amortize research and development (R&D) expenditures under IRC Section 174 for tax years beginning after December 31, 2021. This rule became effective for the Company on January 1, 2022 and resulted in the capitalization of R&D costs of approximately $42.4 million and $42.3 million for tax year ending December 31, 2024 and 2023, respectively. The Company will amortize these costs for tax purposes over 5 years if the R&D was performed in the U.S. and over 15 years if the R&D was performed outside the U.S.

On December 31, 2024, the Company had approximately $422.5 million, $621.8 million and $1,515.7 million of federal, state and foreign net operating loss carryforward, respectively. On December 31, 2023, the Company had approximately $494.1 million, $524.0 million and $1,663.3 million of federal, state and foreign net operating loss carryforward, respectively. The Company also had federal and state research and development tax credit carryforwards $107.8 million and $26.4 million, respectively of as of December 31, 2024. Federal net operating loss carryforward in the amount of $420.9 million may be carried forward indefinitely. The remaining federal and state net operating loss, research and development tax credit carryforwards begin to expire in 2025. The Company's foreign net operating loss carryforwards will begin to expire in 2027.

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. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. The Company may have experienced such ownership changes in the past and may experience ownership changes in the future, as a result of shifts in its stock ownership, some of which are outside the Company's control. Such ownership changes could limit the amount of tax attributes that can be utilized annually to offset future tax liability.

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, 2024 or 2023.

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 2021 through 2023 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.

14. Commitments and Contingencies

The Company has certain non-cancelable purchase obligations related to the manufacturing of drug substance. The Company has agreed to purchase from Bachem Americas, Inc. a significant portion of its requirements for the pegcetacoplan drug substance. Under a commercial supply agreement with NOF Corporation ("NOF"), the Company has agreed to purchase activated polyethylene glycol derivative, or PEG, which is a component of pegcetacoplan. In September 2024, the Company terminated the minimum purchase obligation with NOF for 2025. Under these agreements, as of December 31, 2024, the Company is obligated to pay up to an aggregate of $45.7 million to these vendors. As a result of this termination, the Company incurred an expense of $6.4 million, which is included in cost of sales on the consolidated statements of operations and comprehensive loss. As the amount is not due until January 2026, it is included in other liabilities on the consolidated balance sheet as of December 31, 2024.

In addition, the Company has other non-cancelable purchase agreements as of December 31, 2024, under which it is obligated to pay up to an aggregate of $10.7 million to vendors.

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.

On August 2, 2023, Judith M. Soderberg filed a putative class action in the United States District Court for the District of Delaware against the Company and certain current and former executive officers of the Company (the “Complaint”). The Complaint alleges, among other things, that the defendants violated Sections 10(b) and/or 20(a) of the Exchange Act and Rule 10b-5 promulgated thereunder by misrepresenting and/or omitting certain material facts related to the design of SYFOVRE’s clinical trials and the risks associated with SYFOVRE’s commercial adoption. The Complaint seeks, among other relief, compensatory damages and equitable relief in favor of the alleged class against all defendants, including interest, and reasonable costs and expenses incurred by plaintiffs, including attorneys’ and expert fees.

On October 2, 2023, the defendants moved to transfer the action to the United States District Court for the District of Massachusetts.

On October 23, 2023, the Court appointed Ray Peleckas and Michigan Laborers’ Pension Fund together as Co-Lead Plaintiffs and assigned the action the caption In Apellis Pharmaceuticals, Inc. Securities Litigation, Case 1:23-cv-00834-MN. The Co-Lead Plaintiffs filed an amended complaint on February 8, 2024 (the “Amended Complaint”). The Amended Complaint is brought on behalf of a class of all persons and entities who purchased or otherwise acquired Apellis common stock between January 28, 2021 and July 28, 2023, inclusive, names the Company and Cedric Francois, our chief executive officer, as defendants, and makes similar allegations, asserts the same claims and seeks the same relief as the Complaint. On May 17, 2024, the United States District Court for the District of Delaware approved the motion to transfer to the United States District Court for the District of Massachusetts. The defendants moved to dismiss the Complaint on June 12, 2024, and the Court held oral argument on this motion for November 14, 2024. The Court has not yet ruled on this motion to dismiss.

On December 19, 2024, purported stockholder Patrick Campbell, and on December 30, 2024, purported stockholder Kenneth Olson filed putative stockholder derivative lawsuits in the United States District Court for the District of Massachusetts on behalf of the Company against the Company's directors for breach of fiduciary duty, unjust enrichment, waste, and alleged violation of Section 14(a) of the Exchange Act related to the design of SYFOVRE's clinical trials and the risks associated with SYFOVRE's commercial adoption. The complaints seek monetary and punitive damages, and costs, including attorneys' fees. On January 21, 2025, the cases were consolidated under the caption *In re Apellis Pharmaceuticals, Inc. Derivative Litigation*, No. 1:24-cv-13128-JEK. By the same order, the Court stayed the stockholder derivative litigation pending the Court's ruling on the defendants' motion to dismiss in the securities class action.

The Company's businesses may also be subject at any time to other commercial disputes, product liability claims, personal injury claims, third-party subpoenas or various other lawsuits arising in the ordinary course of business, including intellectual property infringement, employment or investor matters, and the Company expects that this will continue to be the case in the future.

For example, in August 2024, an individual filed a civil action against the Company in the United States District Court in the Northern District of Texas, alleging personal injury claims in connection with the use of SYFOVRE. We moved to dismiss this civil action in September 2024. The Court has not yet ruled on this motion to dismiss, as of the date of issuance of these consolidated financial statements.

The outcome of the matters described above cannot be predicted with certainty and therefore any loss is neither probable nor reasonably estimable. However, the Company intends to vigorously defend against these matters.

15. 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. On January 1, 2024, the shares available for future issuance under the 2017 plan were increased by 4,219,409 shares pursuant to the annual increase described above. As of December 31, 2024, there were 9,726,725 shares available for future grants under the 2017 Plan. In January 2025, the shares available for future issuance under the 2017 plan were increased by an additional 4,219,409 shares.

Additionally, since 2019, 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. The Board of Directors amended the 2020 Plan to add 200,000 shares on January 1, 2024, which increased the total number of shares reserved for issuance to 1,950,000 shares as of January 1, 2024. As of December 31, 2024, there were 528,595 shares available for future grants under the 2020 Plan. No additional shares have been reserved under the 2020 Plan in 2025.

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. On December 31, 2024, 410,940 shares of common stock remained available for issuance pursuant to the ESPP. No additional shares were reserved to the ESPP in 2024 or 2025.

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

	December 31,		
	2024	2023	2022
Shares reserved under 2017 Equity Incentive Plan	20,062	16,989	14,271
Shares reserved under 2017 Employee Stock Purchase Plan	411	553	665
Shares reserved under 2020 Inducement Stock Incentive Plan	1,627	1,638	1,857
Total	22,100	19,180	16,793

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

	Year Ended December 31,		
	2024	2023	2022
Research and development	$ 41,267	$ 45,644	$ 42,052
Selling, general and administrative	72,861	60,301	49,033
Total share-based compensation expense	$ 114,128	$ 105,945	$ 91,085

Stock Options—Options granted to employees vest over 48 months 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.

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 senior 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, 2023	8,664	$ 30.65	6.01	$ 253,933
Granted	685	64.54		
Exercised	(1,080)	13.26		
Forfeited	(221)	49.19		
Outstanding, December 31, 2024	8,048	$ 35.36		
Options exercisable, December 31, 2024	6,713	$ 31.39	4.79	$ 48,477
Expected to vest, December 31, 2024	1,335	$ 55.36	8.25	$ —

The aggregate intrinsic values were calculated as the difference between the exercise price of the options and the fair value of the common stock.

During the years ended December 31, 2024, 2023 and 2022, the Company granted stock options to purchase an aggregate of 0.7 million, 0.8 million and 1.3 million shares of its common stock, respectively with weighted average grant date fair values of $42.61, $34.26 and $23.62, respectively.

The aggregate intrinsic value of options exercised during the years ended December 31, 2024, 2023 and 2022 were $46.0 million, $181.0 million, and $44.8 million, respectively, calculated as the difference between the exercise price of the options and the fair value of the common stock on the respective date of exercise.

As of December 31, 2024, unrecognized compensation expense related to unvested options, was $37.3 million, which the Company expects to recognize over an estimated weighted-average period of 2.3 years.

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

	Year Ended December 31,		
	2024	2023	2022
Risk-free interest rate	3.94 - 4.36%	3.50 - 4.01%	1.15 - 3.37%
Dividend yield	0%	0%	0%
Volatility	71.91 - 77.01%	68.4 - 71.0%	68.3 - 70.4%
Expected terms (years)	3.81 - 6.08	3.81 - 6.08	3.81 - 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.

The following table summarizes the Company's RSU's activity:

	Number of Stock Units (in thousands)	Weighted Average Grant Date Fair Value Per Share
Unvested Balance at December 31, 2023	4,301	$ 47.48
Granted	1,570	62.77
Vested	(1,419)	46.19
Forfeited	(491)	54.10
Unvested Balance at December 31, 2024	3,961	53.19

The fair value of restricted stock units vested during the year ended December 31, 2024, 2023 and 2022, respectively, were $65.5 million, $42.2 million and $15.3 million

As of December 31, 2024, there was approximately $145.9 million of related unrecognized compensation cost which the Company expects to recognize over a remaining weighted average period of 2.4 years.

Employee Stock Purchase Plan— 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, 2024, a total of 141,941 shares of common stock were issued under the ESPP at average per share price of $31.77. During the year ended December 31, 2024, the Company recorded cash received from the issuance of stock to the ESPP of $4.5 million and recorded $2.0 million of stock-based compensation expense related to the ESPP.

16. 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,		
	2024	2023	2022
Numerator:			
Net loss	$ (197,878)	$ (528,628)	$ (652,172)
Denominator:			
Weighted-average number of common shares used in net loss per common share - basic and diluted	123,905	118,678	106,114
Net loss per common share -- basic and diluted	$ (1.60)	$ (4.45)	$ (6.15)

Shares outstanding presented below were excluded from the calculation of diluted net loss per share, prior to the use of the if-converted-method and treasury stock method, as their effect is anti-dilutive (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Convertible notes	2,379	2,379	2,379
Common stock options	8,048	8,664	12,295
Restricted stock units	3,962	4,301	3,572
Total	14,389	15,344	18,246

17. Segment Information

The Company operates as a single operating segment, which is the development and commercialization of treatments across a broad range of diseases driven by complement. The Company defines its segment on the basis in which internally reported financial information is regularly reviewed by CODM to analyze financial performance, make decisions, and allocate resources. The Company's CODM reviews consolidated net loss for purposes of assessing performance, making operating decisions, allocating resources, and planning and forecasting for future periods.

The following table presents information about reported segment revenue, segment loss, and significant segment expenses as provided to the CODM with respect to the Company's single operating segment for the years ended December 31, 2024, 2023 and 2022:

	Year Ended December 31,		
	2024	2023	2022
Revenue	$ 781,367	$ 396,591	$ 75,422
Less:			
Internal research and development costs	91,881	121,931	116,525
Internal selling, general and administrative costs	162,874	176,778	99,750
External commercial costs	229,991	230,166	103,229
External research and development costs	194,422	186,812	228,659
External general and administrative costs	35,327	33,570	25,151
Other segment items (1)	121,842	59,238	38,814
Share-based compensation expense	114,128	105,945	91,085
Interest income	(12,773)	(20,933)	(8,914)
Interest expense	40,391	29,581	32,626
Income tax expense	1,162	2,132	669
Net loss	$ (197,878)	$ (528,629)	$ (652,172)

(1) Other segment items include cost of sales, loss on conversion of debt, and other expenses.

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, 2024. 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, 2024, 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, 2024. In making this assessment, our 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, 2024, our internal control over financial reporting is effective based on those criteria.

Deloitte & Touche LLP, our 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, 2024 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, 2024 materially affected, or were reasonably likely to materially affect, our internal control over financial reporting.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders 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, 2024, 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, 2024, 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, 2024, of the Company and our report dated February 28, 2025, expressed an unqualified opinion on those financial statements.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

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

/s/ Deloitte & Touche LLP

Boston, Massachusetts
February 28, 2025

Item 9B. Other Information.

The following table describes, for the quarterly period covered by this report, each trading arrangement for the sale or purchase of our securities adopted or terminated by our directors and officers that is either (1) a contract, instruction or written plan intended to satisfy the affirmative defense conditions of Rule 10b5-1(c), or a Rule 10b5-1 trading arrangement, or (2) a "non-Rule 10b5-1 trading arrangement" (as defined in Item 408(c) of Regulation S-K):

Name (Title)	Action Taken (Date of Action)	Type of Trading Arrangement	Nature of Trading Arrangement	Duration of Trading Arrangement	Aggregate Number of Securities
Cedric Francois President and Chief Executive Officer	Termination 11/05/2024	Rule 10b5-1 trading arrangement	Sale	(1)	(1)
Jeffrey R Eisele Chief Development Officer	Termination 12/06/2024	Rule 10b5-1 trading arrangement	Sale	(2)	(2)
Jeffrey R Eisele Chief Development Officer	Adoption 12/13/2024	Rule 10b5-1 trading arrangement	Sale	Until 12/31/2025, or such earlier date upon which all transactions are completed or expire without execution	Up to 244,636 shares
Karen L Lewis Chief People Officer	Termination 12/27/2024	Rule 10b5-1 trading arrangement	Sale	(3)	(3)

(1) This trading plan related to 563,194 shares of our common stock and had a scheduled expiration date of 09/03/2025.

(2) This trading plan related to 207,256 shares of our common stock and had a scheduled expiration date of 02/28/2025.

(3) This trading plan related to 101,422 shares of our common stock and had a scheduled expiration date of 03/31/2025.

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 2025 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, 2024, 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, other than the information required by Item 402(v) of Regulation S-K, 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	10-K	001-38276	2/28/2022	4.4	
4.5	Form of Pre-Funded Warrant	8-K	001-38276	2/24/2023	4.1	
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	S-1/A	333-220941	10/13/2017	10.8	

	University of Pennsylvania, as assigned to the Registrant				
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	10-K	001-38276	2/28/2022	10.11
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	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
10.19	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
10.20	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
10.21	Form of Capped Call Transaction Confirmation	8-K	001-38276	5/7/2020	10.1
10.22+	Amendment No. 1 to 2017 Employee Stock Purchase Plan	10-Q	001-38276	11/2/2020	10.1
10.23	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
10.24	Commercial Supply Agreement, dated December 30, 2020, by and between the Registrant and Bachem Americas, Inc.	10-K	001-38276	2/25/2020	10.26
10.25	Sales Agreement, dated as of November 1, 2023 by and between Apellis Pharmaceuticals, Inc. and Cowen and Company, LLC.	8-K	001-38276	11/01/2023	1.1
10.26††	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	4/28/2022	10.1
10.27	Inducement Stock Incentive Plan	S-8	333-236710	2/27/2020	99.1
10.28+	Offer Letter, dated as of December 25, 2022, by and between the Registrant and Baumal Caroline	10-K	001-38276	2/27/2024	10.28

10.30+	Offer Letter, dated as of November 16, 2018, by and between the Registrant and Adam Townsend	10-K	001-38276	2/28/2022	10.30	
10.31	Form of Exchange Agreement	8-K	001-38276	7/8/2021	10.1	
10.32	Form of Restricted Stock Unit Agreement under the 2017 Stock Incentive Plan	10-K	001-38276	2/21/2023	10.33	
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
97.1	Dodd-Frank Compensation Recovery Policy	10-K	001-38276	2/27/2024	97.1	
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, 2025

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, 2025
/s/ Timothy E. Sullivan **Timothy E. Sullivan**	Chief Financial Officer and Treasurer (Principal Financial Officer)	February 28, 2025
/s/ Jim Chopas **Jim Chopas**	Vice President, Corporate Controller and Chief Accounting Officer (Principal Accounting Officer)	February 28, 2025
/s/ Gerald Chan **Gerald Chan**	Director	February 28, 2025
/s/ A. Sinclair Dunlop **A. Sinclair Dunlop**	Director	February 28, 2025
/s/ Alec Machiels **Alec Machiels**	Director	February 28, 2025
/s/ Stephanie M. O'Brien **Stephanie M. O'Brien**	Director	February 28, 2025
/s/ Paul Fonteyne **Paul Fonteyne**	Director	February 28, 2025
/s/ Keli Walbert **Keli Walbert**	Director	February 28, 2025

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Directors

Cedric Francois, M.D., Ph.D.

Gerald Chan, D.Sc.

A. Sinclair Dunlop

Paul Fonteyne

Alec Machiels

Stephanie Monaghan O'Brien

Keli Walbert

Craig Wheeler

Executive Officers

Cedric Francois, M.D., Ph.D.

President & Chief Executive Officer

Caroline Baumal, M.D.

Chief Medical Officer

Jim Chopas

Vice President, Chief Accounting Officer

Mark Delong

Chief Business & Strategy Officer

Pascal Deschatelets, Ph.D.

Chief Scientific Officer

Nur Nicholson

Chief Technical Operations Officer

Timothy Sullivan

Chief Financial Officer & Treasurer

David Watson

General Counsel & Secretary

Stock Listing

Our common stock is traded on Nasdaq Global Select Market under the symbol "APLS".

Investor Information

You may obtain a copy of any of the exhibits to our Annual Report on Form 10-K free of charge. These documents are available on our website at www.apellis.com or by contacting our Investor Relations.

Requests for information about Apellis Pharmaceuticals, Inc. should be directed to:

Investor Relations
investors@apellis.com

Annual Meeting

The annual meeting of stockholders will be held virtually via the Internet at the time and website stated below.

Tuesday, June 3, 2025
9:30 am ET

https://www.proxydocs.com/APLS

Corporate Counsel

Wilmer Cutler Pickering Hale and Dorr LLP
Boston, Massachusetts

Independent Registered Public Accounting Firm

Deloitte & Touche LLP
Boston, Massachusetts

Transfer Agent and Registrar

The transfer agent is responsible, among other things, for handling stockholder questions regarding lost stock certificates, address changes, including duplicate mailings and changes in ownership or name in which shares are held. These requests may be directed to the transfer agent at the following addresses:

Equiniti Trust Company, LLC
55 Challenger Road, Floor 2
Ridgefield Park, NJ 07660
Phone: (800) 937-5449
Email: helpAST@equiniti.com
Website: www.equiniti.com

Apellis Pharmaceuticals, Inc.
100 Fifth Avenue
Waltham, MA 02451
(617) 977-5700 Main Office
Email: info@apellis.com
www.apellis.com