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, 2022

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 001-39661

ATEA PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its Charter)

Delaware	**46-0574869**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
225 Franklin Street, Suite 2100	
Boston, MA	**02110**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (857) 284-8891

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, $0.001 par value per share	AVIR	The 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 Section 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	☐	Smaller reporting company	☐
Emerging growth company	☐		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 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 Act). YES ☐ NO ☒

As of June 30, 2022, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the last reported sales price for the registrant's common stock, par value $0.001 per share, on the Nasdaq Global Select Market on such date, was approximately $537,283,731.

The number of shares of Registrant's Common Stock outstanding as of February 25, 2023 was 83,341,574.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2023 Annual Meeting of Stockholders, which the registrant intends to file with the Securities and Exchange Commission within 120 days after the end of the registrant's fiscal year ended December 31, 2022, are incorporated by reference into Part III of this Annual Report on Form 10-K.

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our clinical development timelines and results and other future conditions. The words “aim,” “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “goal,” “intend,” “may,” "on track," “plan,” “possible,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would” or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

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

- our expectations relating to clinical trials for our product candidates, including projected costs, study designs and the timing for initiation, recruitment, completion, and reporting top-line data;
- the potential therapeutic benefits of our product candidates and the potential indications and market opportunities therefor;
- the potential of bemnifosbuvir to retain antiviral activity against circulating COVID-19 variants of concern and to treat COVID-19;
- the safety profile and related adverse events of our product candidates;
- our plans to research, develop and commercialize our current and future product candidates;
- the potential benefits of any future collaboration we may enter into;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of any products for which we may receive marketing approval;
- our manufacturing and commercialization capabilities and strategy;
- our estimates regarding future revenue, expenses and results of operations;
- the progress of, timing of and amount of expenses associated with our research, development and commercialization activities;
- our future financial position, capital requirements, needs for additional financing and the availability of such financing;
- our business strategy;
- developments relating to our industry and our competitors, including competing treatments and vaccines for diseases we are treating;
- our expectations regarding federal, state and foreign laws and regulations;
- our ability to attract, motivate, and retain key personnel; and
- the impact on our business as COVID-19 becomes endemic.

These forward-looking statements are based on management's current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Factors that may cause actual results to differ materially from current expectations include the initiation, execution and completion of clinical trials, uncertainties surrounding the timing of availability of data from our clinical trials, ongoing discussions with and actions by regulatory authorities, our development activities and those other factors we discuss in Part I, Item 1A. "Risk Factors." You should read these risk factors and the other cautionary statements made in this report as being applicable to all related forward-looking statements wherever they appear in this report. The risk factors are not exhaustive and other sections of this report may include additional factors which could adversely impact our business and financial performance. Given these uncertainties, you should not rely on these forward-looking statements as predictions of future events. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

As used in this Annual Report on Form 10-K, unless otherwise specified or the context otherwise requires, the terms "we," "our," "us," and the "Company" refer to Atea Pharmaceuticals, Inc. and its subsidiary. All brand names or trademarks appearing in this Annual Report on Form 10-K are the property of their respective owners.

SUMMARY RISK FACTORS

Our business is subject to numerous risks and uncertainties, including those described in Part I, Item 1A. “Risk Factors” in this Annual Report on Form 10-K. The principal risks and uncertainties affecting our business include the following:

- There is significant uncertainty around our development of bemnifosbuvir as a potential treatment for COVID-19.
- We are highly dependent on our management, directors and other key personnel.
- We may expend resources in anticipation of potential clinical trials and commercialization of bemnifosbuvir, which we may not be able to recover if bemnifosbuvir is not approved for the treatment of COVID-19, we are not successful at commercializing bemnifosbuvir or bemnifosbuvir is rendered inferior or obsolete due to rapid changes in COVID -19 epidemiology as a result of the emergence of new SARS-CoV-2 variants or subvariants.
- The market for new therapeutics for the treatment of COVID-19 may be reduced, perhaps significantly, if vaccines and current therapeutics remain effective in minimizing serious consequences of the disease.
- If approved, bemnifosbuvir will face significant competition from other treatments for COVID-19 that are currently marketed or are in development.
- The COVID-19 pandemic and future variant fueled pandemic surges may materially and adversely affect our business opportunities, clinical trials and financial results.
- We have a limited operating history and no history of successfully developing or commercializing any approved antiviral products, which may make it difficult to evaluate the success of our business to date and to assess the prospects for our future viability.
- We have incurred significant operating expenses since inception. We expect our expenditures will increase for the foreseeable future. We have no products that have generated any commercial revenue and we may never again achieve or maintain profitability.
- We will require substantial additional financing, which may not be available on acceptable terms, or at all. A failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our product development or commercialization efforts.
- Our ability to use our net operating loss carryforwards and other tax attributes to offset taxable income may be subject to certain limitations.
- Our business is highly dependent on the success of our most advanced product candidates, including bemnifosbuvir. If we fail to successfully develop bemnifosbuvir for the treatment of COVID-19 or the combination of bemnifosbuvir and ruzasvir for the treatment of hepatitis C or we are unable to obtain regulatory approval or successfully commercialize any of our product candidates, or are significantly delayed in doing so, our business will be harmed.
- The regulatory approval processes of the US Food and Drug Administration (“FDA”) and comparable foreign regulatory authorities are lengthy, expensive, time-consuming and inherently unpredictable.
- Clinical development, including enrollment of patients in clinical trials, is an expensive, lengthy and uncertain process. We may encounter substantial delays and costs in our clinical trials, or may not be able to conduct or complete our clinical trials on the timelines we expect, if at all.
- We intend to develop certain of our product candidates in combination with other product candidates that we discover or acquire, which exposes us to additional risks.
- Our product candidates may be associated with serious adverse events, undesirable side effects or have other properties that could halt their clinical development, prevent their

regulatory approval, limit their commercial potential or result in significant negative consequences.

- We currently conduct and may in the future conduct clinical trials of our product candidates in sites outside the United States ("US"). The FDA may not accept data from trials conducted in foreign locations.
- Interim, topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more data become available and are subject to audit and verification procedures that could result in material changes in the final data.
- We may not be successful in our efforts to identify and successfully develop additional product candidates.
- Risks related to healthcare laws and other legal compliance matters may materially and adversely affect our business and financial results.
- Risks related to commercialization may materially and adversely affect our business and financial results.
- Risks related to manufacturing and our dependence on third parties may materially and adversely affect our business and financial results.
- Risks related to intellectual property may materially and adversely affect our business and financial results.
- We have only a limited number of employees, which may be inadequate to manage and operate our business.
- Our business and operations may suffer in the event of system failures, security breaches, deficiencies or intrusions which could materially affect our results.
- We may need to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.
- We may engage in acquisitions or strategic partnerships that could disrupt our business, cause dilution to our stockholders, reduce our financial resources, cause us to incur debt or assume contingent liabilities, and subject us to other risks.
- We or the third parties upon whom we depend may be adversely affected by natural disasters or other unforeseen events resulting in business interruptions and our business continuity and disaster recovery plans may not adequately protect us from such business interruptions.
- Increased attention to, and evolving expectations for, environmental, social, and governance (“ESG”) initiatives could increase our costs, harm our reputation, or otherwise adversely impact our business.
- Litigation against us could be costly and time-consuming to defend and could result in additional liabilities.
- Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.
- Risks related to our common stock may materially and adversely affect our stock price.
- If we fail to maintain effective internal control over financial reporting and effective disclosure controls and procedures, we may not be able to accurately report our financial results in a timely manner or prevent fraud, which may adversely affect investor confidence in our company.

PART I

Item 1. Business.

Overview

We are a clinical-stage biopharmaceutical company focused on discovering, developing, and commercializing antiviral therapeutics to improve the lives of patients suffering from serious viral infections. We are developing our lead product candidate, bemnifosbuvir, for the treatment of COVID-19, the disease caused by infection with Severe Acute Respiratory Syndrome Coronavirus 2 ("SARS-CoV-2") and its variants. We are also developing bemnifosbuvir in combination with ruzasvir for the treatment of Hepatitis C ("HCV").

COVID-19 has caused a global health crisis resulting in millions of deaths and lingering medical issues for many survivors. While there have been many rapid advances in the prevention and treatment of COVID-19, due to the limitations of the current vaccine and treatment options, there remains a significant unmet medical need for large numbers of high-risk individuals both in the US and globally. Our COVID-19 strategy is centered on the development of bemnifosbuvir as a monotherapy and potentially as a part of a COVID-19 therapy that combines bemnifosbuvir with another antiviral agent and focuses on these high-risk patients for whom current vaccines and treatments remain inadequate. Our goal is to deliver a safe, effective, and convenient treatment option for individuals that remain vulnerable to hospitalization and death as a result of infection with SARS-CoV-2.

Even with the availability of vaccines and therapeutics, COVID-19 is the third leading cause of mortality in the US after only heart disease and cancer. As of February 15, 2023, the CDC reported that more than 400 persons a day are dying in the US from COVID-19 or related complications. More than 75% of these persons are 65 years and older. Additionally, it has been reported as recently as February 15, 2023, persons 60 years and older account for ~70% of current US hospitalizations associated with COVID-19.

While the US government has recently announced plans to end the declaration of a public health emergency associated with COVID-19, COVID-19 is expected to remain a serious endemic threat for an indefinite future period. The reasons contributing to the likelihood of COVID-19 remaining an endemic threat include: (1) viral transmission before symptom onset; (2) uneven global rollout of vaccinations; (3) ongoing vaccine hesitancy; (4) limited duration of immunity conferred by both natural infection and vaccination; (5) limited vaccine efficacy against certain SARS-CoV-2 variants; (6) limitations of current oral antivirals such as drug-drug interactions, safety concerns and tolerability; (7) uncertain impact of vaccines on transmission; (8) continuing evolution of the virus evading endogenous and vaccine-induced immunity; and (9) diminution of virus transmission mitigation behaviors, such as wearing masks and social distancing.

The continued emergence of SARS-CoV-2 variants that may have greater transmissibility and may cause more severe disease, combined with the diminution of virus mitigation behaviors among others in the general population, together with the consequences that are expected to associate with the end of the public health emergency leave patients for whom current therapeutics are limited particularly vulnerable to the virus and related disease. In view of these factors, we are developing bemnifosbuvir as a potential therapy to meet the needs of these vulnerable patients.

As COVID-19 continues to persist as a serious global endemic disease, we believe that the COVID-19 therapeutic market will remain a multi-billion-dollar opportunity for many years to come with the US continuing to comprise the most significant commercial market. In the US, we anticipate that the COVID-19 commercial market will soon transition from a single government payer to more traditional payer channels such as Medicare, Medicaid and private commercial insurance. We anticipate a major consideration for determining reimbursement by these third party payers will be a cost/value analysis that is driven in part by the economic burden of hospitalization, especially for at-risk populations.

Bemnifosbuvir

We utilized our team's expertise and experience, gained from decades of developing innovative antiviral treatments, to design bemnifosbuvir, an investigational, proprietary, potent, and selective, nucleotide polymerase inhibitor, which may be developed as each of a monotherapy and in combination with other antiviral agents. Bemnifosbuvir (AT-527) has been derived from our internal discovery program that combines unique nucleotide scaffolds with novel double prodrugs for the purpose of inhibiting the enzymes central to viral replication. Utilizing this double prodrug moiety approach, we believe that we have been able to maximize formation of the active metabolite of bemnifosbuvir thereby creating an oral antiviral product candidate that is designed to prevent replication of single stranded RNA ("ssRNA") viruses while avoiding toxicity to host cells. In nonclinical studies we have demonstrated that bemnifosbuvir has a unique mechanism of action that includes both RNA-dependent RNA polymerase ("RdRp") chain termination and inhibition of the nidovirus RdRp associated nucleotidyltransferase ("NiRAN") of the SARS-CoV-2 virus and variants. By targeting these highly conserved sites through this unique dual mechanism of action, bemnifosbuvir has the potential to create a high barrier to resistance. Additionally, in *in vitro* studies we have conducted, bemnifosbuvir maintained its antiviral activity across COVID-19 variants of concern ("VOC"), including all Omicron subvariants tested.

COVID-19 Clinical Studies

In November 2022, we initiated SUNRISE-3, a global, multicenter, randomized, double-blind, placebo-controlled Phase 3 clinical trial. SUNRISE-3 is evaluating bemnifosbuvir (550 mg twice-daily ("BID") for five days) in at least 1500 high-risk non-hospitalized patients with mild or moderate COVID-19. The trial will be conducted at clinical trial sites in the US, Europe, Japan, and other regions of the world. The patient population will consist of those at the highest risk for disease progression, including patients ≥ 80 years old, patients ≥ 65 years old with one or more major risk factors, and immunocompromised patients ≥ 18 years old, all regardless of COVID-19 vaccination status.

SUNRISE-3 is designed to evaluate bemnifosbuvir as monotherapy (primary analysis) but will also explore the effect of combination therapy in a smaller sub-set of patients who receive an antiviral drug along with bemnifosbuvir (secondary analysis). The trial will include two populations derived from the type of standard of care ("SOC") received: 1) "supportive care population" (those patients who do not qualify for an approved antiviral treatment or where antivirals are not locally available) which will assess bemnifosbuvir given as monotherapy (primary analysis) and 2) "combination antiviral population" which will assess combination therapy if the SOC includes treatment with other compatible antiviral drugs against COVID-19 (secondary analysis). Patients are being randomized 1:1 to receive either bemnifosbuvir 550 mg BID plus locally available SOC or placebo BID plus locally available SOC for five days.

The primary endpoint of the SUNRISE-3 study is all-cause hospitalization or death through Day 29 in at least 1,300 patients in the supportive care population and is powered to detect a clinically meaningful reduction in hospitalization/death versus placebo in this population. By enriching the patients enrolling in the trial with those who are at the highest risk for disease progression, we are targeting rates of hospitalization/death of ~4-6%. An interim analysis will be conducted by an independent data safety monitoring board ("DSMB") after 60% patient enrollment in the arm of the study enrolling the supportive care population. Secondary endpoints in each of the supportive care patient population and the combination antiviral population include COVID-19 complications, medically attended visits, symptom rebound/relapse and viral load rebound.

Data from prior studies of bemnifosbuvir that we have relied upon to support the design of SUNRISE-3 includes results from the Phase 3 clinical trial referred to as MORNINGSKY that was closed out early along with results from Phase 1 drug-drug interaction ("DDI") studies. While the primary endpoint of the MORNINGSKY study, time to symptom alleviation, was not achieved, the results from MORNINGSKY demonstrated a 71% reduction in hospitalization (2.9% versus 10%) (p=0.047, unadjusted, exploratory; secondary endpoint) in the bemnifosbuvir arm (n=137) versus placebo (n=70). The patients enrolled in the MORNINGSKY trial consisted of a broad outpatient population including 47% who were high risk, 28% who were vaccinated, and 56% who were seropositive at baseline. In a subgroup analysis in

patients greater than 40 years old, the reduction in hospitalization in the bemnifosbuvir arm of the MORNINGSKY trial was even greater at 82%.

To date, five clinical DDI studies have been completed and demonstrated an overall low DDI potential associated with bemnifosbuvir including no dosage adjustment needed for co-administration of bemnifosbuvir with drugs that are CYP3A substrates or for drugs that are sensitive substrates of efflux and hepatic uptake transporters. CYP3A is an enzyme that metabolizes many classes of medicines and supplements, and the sensitive substrates of efflux and hepatic uptake transporters regulate cellular trafficking of many drugs that are commonly prescribed to patients at high risk for COVID-19.

In these DDI studies, bemnifosbuvir was administered with index drugs for CYP3A4 (midazolam), P-glycoprotein (digoxin, cyclosporine, carbamazepine), breast cancer resistance protein and organic anion transporter polypeptide 1B1 (rosuvastatin). Based on low potential for drug interaction, we believe bemnifosbuvir has the potential to be co-administered with commonly prescribed therapeutics that are often taken for other conditions, especially in vulnerable patient populations who are at high risk for disease progression to severe COVID-19.

In parallel to conducting our SUNRISE-3 clinical trial, we are engaging in efforts to discover a protease inhibitor product candidate that we may combine with bemnifosbuvir for the treatment of specific COVID-19 patient populations that are unable to mount immune response and require combination therapy. We have conducted *in vitro* studies that have demonstrated an additive antiviral effect when bemnifosbuvir was combined with antivirals from the protease inhibitor class, including nirmatrelvir. The data that we anticipate obtaining from the SUNRISE-3 clinical trial in the subset of patients who receive combination therapy will be, we believe, the first clinical data evaluating the combination of bemnifosbuvir and certain other currently authorized antiviral treatments.

Combination Therapy

Combination therapy utilizing multiple direct acting antivirals with differing mechanisms of action is an established strategy that has been historically successful in treating many life-threatening viral diseases, including human immunodeficiency virus (“HIV”), hepatitis B virus (“HBV”) and HCV. Nucleos(t)ide analogs are the backbone of many of these successful combination therapies. Advantageously, drug combinations can simultaneously target multiple points in the viral replication cycle with the effect of increasing antiviral activity and can also combat resistance that may develop over time with use of single agent drugs.

Hepatitis C Virus (HCV) Clinical Studies

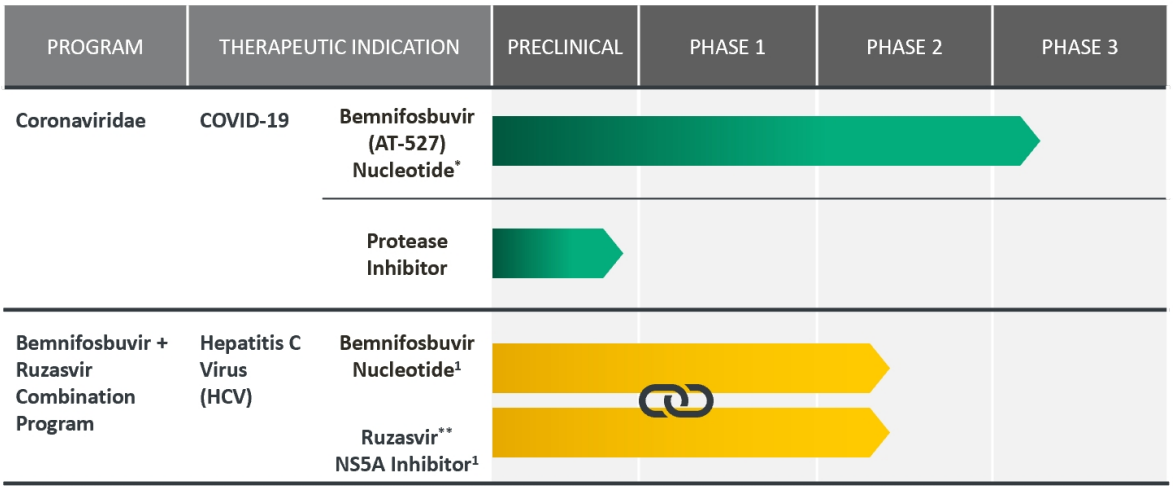
For the treatment of chronic HCV infection, we are advancing the combination of bemnifosbuvir and ruzasvir, an investigational NS5A inhibitor. Approximately 58 million people globally, including ~2.4 million in the US, are living with chronic HCV infection. The World Health Organization ("WHO") reports a global incidence of 1.5 million cases per year and 399,000 deaths per year. The US HCV prevalence is expected to remain constant over the coming years as rising HCV incidence offsets the number of new patients treated.

We believe that the combination of bemnifosbuvir and ruzasvir has the potential to improve upon the current standard of care by offering a differentiated short duration, pan-genotypic protease-sparing regimen for HCV-infected patients with or without cirrhosis.

During the second quarter of 2023, we plan to initiate enrollment of a Phase 2 clinical trial of bemnifosbuvir in combination with ruzasvir in treatment-naïve, HCV-infected patients either without cirrhosis or with compensated cirrhosis. This study is designed to evaluate the safety and efficacy of the pan-genotypic combination consisting of 550 mg once daily ("QD") of bemnifosbuvir and 180 mg QD of ruzasvir after eight weeks of treatment. Approximately 280 HCV-infected, treatment-naïve patients across all genotypes, including a lead-in cohort of approximately 60 patients, are expected to be enrolled in this Phase 2 clinical trial. The primary endpoints of the study are safety and sustained virologic response ("SVR") at Week 12 post-treatment. Other virologic endpoints include virologic failure, SVR at Week 24 post-treatment and resistance.

Our Development Pipeline

The following table summarizes our orally administered antiviral product candidate pipeline. We have full global rights to commercialize all of our product candidates in all indications.



*Bemnifosbuvir (generic name for AT-527) is a double prodrug nucleotide analog. ** Worldwide exclusive license for all uses from Merck.

1. Bemnifosbuvir and ruzasvir have each separately generated clinical results and will be developed as a combination for HCV.

Dengue and RSV

In February 2023, after advancing AT-752 to a Phase 2 clinical trial, we have determined not to pursue further clinical development of AT-752 for the treatment and prophylaxis of dengue. This action was taken due to the long timelines anticipated for patient enrollment, expected clinical operational challenges, including the challenge of successfully administering an antiviral very shortly after infection which is not feasible with the current diagnostic tests, and estimated resource burdens, including substantial costs, associated with the further clinical development of an antiviral for each of the treatment and prophylaxis of dengue.

We have also recently determined not to further pursue our discovery efforts to identify a product candidate for the treatment of respiratory syncytial virus ("RSV"). This action was taken to facilitate enhanced focus of our management team and to deploy our other resources on those therapeutic indications where our programs are more advanced.

We believe we are well capitalized to advance our current programs. We had $646.7 million in cash, cash equivalents and marketable securities at December 31, 2022. Based on our current plans, we anticipate these financial resources will allow us to advance our current and planned clinical programs to and through key inflection points and to fund our activities into 2026.

Our Strategy

Our goal is to become a global leader in the discovery, development, and commercialization of novel antiviral therapies for serious or life-threatening viral infections. We intend to achieve this goal by pursuing the following strategies:

Deploy our expertise and experience particularly our depth of knowledge with respect to nucleos(t)ide analogs to discover and develop novel or differentiated direct acting antivirals that have the potential to meet unmet medical needs or improve the current standard of care. We have assembled and are utilizing the expertise and experience of a team with a demonstrated track

record of efficiently and successfully discovering, developing, obtaining global regulatory approvals and commercializing innovative direct acting oral antiviral therapeutics**.** Our team has very specific expertise in the identification of unmet patient needs, virology, medicinal chemistry, particularly nucleos(t)ide chemistry and optimization, drug discovery, preclinical and clinical development, regulatory affairs and commercialization. We have relied on that expertise to:

- discover bemnifosbuvir, an investigational, novel, double prodrug nucleotide analog, which we are developing for the treatment of COVID-19 and HCV; and

- identify and in-license ruzasvir, an investigational NS5A inhibitor, that we intend to evaluate in combination with bemnifosbuvir for the treatment of HCV.

Additionally, we are using that expertise to:

- conduct our clinical trials, including the Phase 3 clinical trial SUNRISE-3, for the treatment of COVID-19, which is currently enrolling patients, and a Phase 2 clinical trial that we expect will initiate enrollment of patients in the second quarter of 2023 for the treatment of HCV; and

- design an optimized second-generation protease inhibitor that we anticipate to combine with bemnifosbuvir for the treatment of COVID-19.

Develop bemnifosbuvir (AT-527) as monotherapy for COVID-19 to address key limitations of current therapies and explore combination therapy for specific patient populations. Bemnifosbuvir, is an investigational, orally administered, non-mutagenic, non-teratogenic, direct-acting antiviral agent being evaluated in our Phase 3 SUNRISE-3 clinical trial as monotherapy and in combination with other antivirals as a part of the locally available SOC. Supportive data from MORNINGSKY showed a 71% lower risk of hospitalization in the bemnifosbuvir arm versus placebo (p=0.047, unadjusted, exploratory; secondary endpoint). In a subgroup analysis in patients greater than 40 years old, the reduction in hospitalization was even greater at 82%.

We are developing bemnifosbuvir for COVID-19 to address the current highest unmet medical need. Specifically, we are targeting the most vulnerable patient populations who are at the greatest risk for disease progression to severe COVID-19 or mortality, and for whom there are currently the fewest treatment options. With currently available oral antivirals, there are serious limitations that minimize or eliminate the suitability of use in certain patient populations and monoclonal antibodies are no longer effective against COVID-19 variants and subvariants. These limitations include DDIs with commonly prescribed medications such as seizure medications, anti-psychotics and anti-coagulants. In addition, currently available vaccines have also presented limitations, including waning immunity and failure to mount immune response in specific populations.

We believe the potential product profile we are targeting for bemnifosbuvir with potential low risk for DDIs would fulfill an unmet need for an oral antiviral for COVID-19. If realized in clinical studies and if bemnifosbuvir is approved, we believe this potential profile may enable bemnifosbuvir to become a cornerstone of both monotherapy and combination oral therapy for the treatment of COVID-19.

In addition to the development of bemnifosbuvir as a monotherapy, we are advancing the development of COVID-19 combination therapy for specific immunocompromised populations. *In vitro* combinations of bemnifosbuvir with authorized direct acting antivirals, including protease inhibitors, have demonstrated additive antiviral activity and we continue to advance our internal protease inhibitor program for future combination therapy with bemnifosbuvir.

Advance a pan-genotypic regimen of bemnifosbuvir and ruzasvir for HCV that has the potential to improve the standard of care. Despite the availability of direct acting antiviral oral combination regimens for the treatment of HCV, there remains a large, underserved, HCV patient population which continues to grow in the US. A large portion of this increase in incidence is attributable to the opioid crisis, IV drug use, and HCV reinfection, especially among younger adults. Clinical studies that Merck conducted with ruzasvir and clinical studies of bemnifosbuvir we have conducted each demonstrated potent antiviral activity and were well tolerated by HCV-infected patients. Synergy of the combination of bemnifosbuvir and ruzasvir in inhibiting HCV replication has also been observed *in vitro*. We expect to initiate enrollment

of a Phase 2 clinical trial evaluating the combination of bemnifosbuvir and ruzasvir during the second quarter of 2023. We believe that the combination of bemnifosbuvir and ruzasvir with a short treatment duration and protease inhibitor-free regimen, if successfully developed and approved, has the potential to benefit the expanding populations of HCV-infected patients in the US and globally.

Maximize the value of our product candidates by retaining rights and selectively seeking advantageous collaborations to enhance our global commercialization reach. We generally intend to retain global development and commercialization rights to our product candidates, which we believe will allow us to retain the greatest potential value of our product portfolio. However, we may opportunistically enter into commercialization license agreements or collaborations when and where we believe there is an opportunity, particularly outside the US, to gain specific market expertise and other commercialization resources without requiring us to build significant commercial infrastructure.

Remain opportunistic for in-licensing opportunities to augment our pipeline. In addition to our internal research activities which are currently focused on the potential discovery and preclinical development of a second-generation protease inhibitor product candidate, we plan to remain opportunistic in the evaluation of third party clinical-stage antiviral drug candidates that we may in-license to augment our existing pipeline. Utilizing our scientific expertise, we will continue to evaluate in-licensing opportunities that would allow us to address significant unmet medical need or where we anticipate we could substantively improve upon the current standard of care.

Our Team

Our management team has significant experience discovering, developing, and commercializing antiviral therapies for life-threatening viral infections. Our Founder, Chairman, and Chief Executive Officer, Jean-Pierre Sommadossi, Ph.D., has over 30 years of scientific, operational, strategic, and management experience in the biopharmaceutical industry. Dr. Sommadossi has authored over 180 peer-reviewed publications and holds more than 135 US patents related to antiviral and cancer therapeutics. Dr. Sommadossi was the principal founder of Idenix Pharmaceuticals, Inc. (“Idenix”), which was acquired by Merck in 2014, and a co-founder of Pharmasset, Inc. (“Pharmasset”), which was acquired by Gilead Sciences, Inc. in 2012.

We have assembled an experienced management and scientific team with a track record of success in the field of antiviral drug development, many of whom have worked together previously. Our team has significant expertise in nucleos(t)ide chemistry, biochemistry and virology and has applied that expertise towards the discovery and development of innovative antiviral treatments, including Epivir, Sovaldi, Tyzeka, Valtrex, Wellferon, Videx, Reyataz, Sustiva, Mavyret, Xofluza, Relenza, Zerit, Zepatier, Epclusa, Harvoni and Veklury. Members of our team have held senior positions at AstraZeneca plc, Merck, GlaxoSmithKline plc, Chiron, Novartis International AG, Biogen, F. Hoffmann La Roche, Abbvie, Bristol Myers Squibb, Shire, Biohaven Pharma, Pharmasset, Idenix, Valeant Pharmaceuticals International, Gilead Sciences, Inc. and Alnylam Pharmaceuticals.

Antiviral Therapy

Background on viruses

Viruses are cellular parasites that lack the machinery required to survive and replicate on their own and can only replicate using a host cell’s replication process. Unlike living organisms, such as humans, that use DNA as the basis for their genetic material, viruses can use either DNA or RNA. Approximately 70% of all viruses are RNA viruses. RNA viruses can be single stranded (ssRNA) viruses or double-stranded (dsRNA), viruses, depending on the type of RNA used as the genetic material.

Viruses have two primary components: nucleic acid (single or double stranded RNA or DNA) and a protective shell (the capsid). Some viruses may also have a lipid bilayer (the envelope) surrounding the capsid, an additional membrane derived from host cell membranes that contains viral proteins. A virus encased within a lipid bilayer is known as an enveloped virus, while a virus without this bilayer is called a non-enveloped virus. Enveloped ssRNA viruses are the more prevalent cause of severe human viral disease. Each of SARS-CoV-2, a coronavirus belonging to the coronaviridae family, and hepatitis C virus, a flavivirus, are enveloped ssRNA viruses.

Viral infection occurs and the viral replication process begins when a virus attaches itself to a specific receptor site on the host-cell membrane through attachment proteins. The viral replication mechanism is dependent upon whether the virus is an RNA or DNA virus. Most DNA viruses use host cell proteins and enzymes to make additional DNA that is used to copy the viral genome or is transcribed to messenger RNA ("mRNA"). RNA viruses use their RNA as a template for synthesis of viral genomic RNA and mRNAs. The mRNAs encode both nonstructural proteins responsible for viral replication and transcription and structural proteins responsible for viral assembly. Finally, the newly created virus particles ("virions"), are released from the host cell in order to repeat the infection and replication cycle. RNA viruses can be particularly challenging to treat, as the error rates around the viral RNA polymerase directed RNA synthesis cause high mutation rates during replication, creating variants and resistance challenges for antiviral therapies.

Viral polymerase as an antiviral target

The viral polymerase, which is the single protein present in all RNA viruses, is a key enzyme in the replication of viruses making it an attractive target for antiviral therapeutics. Among other things, the core structural features of viral polymerase are highly conserved across different viruses, making drugs targeted to the polymerase less susceptible to the effects of viral mutation and resistance. There are four types of viral polymerase, depending upon the virus and its genomic makeup:

- RNA-dependent RNA polymerase (RdRp): All ssRNA viruses, including SARS-CoV-2 and HCV, depend on the RdRp, encoded in the viral genome, for replication and transcription. Since these enzymes are not present in the host cell, this facilitates the design of selective inhibitors of viral replication, which target viral but not host cell polymerases.
- DNA-dependent DNA polymerase ("DdDp"): DdDp is used by DNA viruses to replicate their genome.
- RNA-dependent DNA polymerase ("RdDp or reverse transcriptase"): Reverse transcriptase is used by certain DNA or RNA viruses, such as HBV and HIV-1, to replicate their genomes.
- DNA-dependent RNA polymerase (DdRp): DdRp is used by DNA viruses to transcribe mRNA from DNA templates during replication.

As viral RNA polymerase-based synthesis does not occur in human host cells, antiviral drug development for RNA viruses focuses on identifying selective drug-like molecules that target viral RNA polymerase. Advances in technology have enabled intensive structural and functional studies of viral RNA polymerase including the identification in the case of SARS-CoV-2 of nidovirus RdRp associated nucleotidyltransferase (NiRAN) and have opened avenues for the development of new and more effective antiviral therapies.

Viral resistance and variants

A major challenge to the development of direct acting antivirals is the emergence of viral resistance. Resistance is a function of a virus' ability to genetically mutate and become less susceptible to certain antiviral therapies over time. In the case of RNA viruses, which lack proofreading abilities, the rate of mutation is substantially higher than DNA viruses and can occur at six orders of magnitude greater than the rate of mutation of host cells.

Another anticipated and naturally recurring consequence of viral mutations is the emergence of new variants. Variants are new strains of the original virus with genetic codes that are unique from the original virus. As a result of the unique genetic code, variants may have more or less transmissibility or virulence and may result in more severe disease than the original virus. Additionally, because of the changes in the genetic code of the variant, the effectiveness of vaccines and therapeutics may be reduced to the point of obsolescence.

SARS-CoV-2 has proven to be able to mutate quickly with more than six million variants identified since fall 2020. A number of these variants have been designated by WHO and Centers for Disease Control and Prevention ("CDC") as Variants of Interest ("VOI") because there is evidence of increased transmissibility, more severe disease, reduced effectiveness of vaccines or antibodies, or diagnostic detection failures. However, these strains may only appear in isolated regions and have not yet spread to

other countries. WHO and CDC have also identified a number of VOC which express similar attributes to VOIs but are more likely to be responsible for greater disease severity across the globe. Previously identified VOCs included Alpha, Beta, Gamma, and Delta while the currently circulating VOC is Omicron, which includes BA.1, BA.2, BA.3 BA.4, BA.5 and descendent lineages.

Globally, from January 10, 2023 to February 6, 2023 it was reported that 99.6% of SARS-CoV-2 sequences were the Omicron VOC. Among the Omicron VOC, BA.5 and its descendent lineages dominated globally, accounting for 53.9% prevalence of all submitted sequences during the January 16 to January 22 January 2023 timeframe. In light of the widespread transmission of the Omicron VOC across the globe, WHO has added a new category to its variant tracking system, "Omicron subvariants under monitoring," which may require prioritized attention and monitoring. Current Omicron subvariants under monitoring include BF.7, BQ.1, BA.2.75, CH.1.1, XBB, XBB.1.5, and XBF.

Given the mutagenic nature of SARS-CoV-2, we expect that the evolution of the virus will continue with more variants emerging and presenting new and varied health challenges. The continued emergence of dominant SARS-CoV-2 variants is a key contributor to COVID-19 evolving from a pandemic to an endemic threat where the virus will still be circulating, with surges from time to time.

Nucleos(t)ide analogs and prodrugs

Nucleic acids are composed of naturally occurring chemical compounds termed nucleosides and nucleotides and are the main information-carrying molecules of the cell that determine the inherited characteristics of human and viral genetic material by directing the process of protein synthesis. The two main classes of nucleic acids are DNA and RNA. Nucleos(t)ide analogs are synthetic compounds that mimic the structure of naturally occurring nucleosides and nucleotides that target the viral polymerase directly so that it mistakenly incorporates these analogs into nascent nucleic acids, causing inhibition of viral replication. Nucleos(t)ide analogs, compared to other classes of antiviral therapies, have a high barrier to viral resistance due to the conservation of the structure of the polymerase that is required to produce viable virions.

Prodrugs are biologically inactive compounds which are employed to improve drug delivery, bypass rate limiting activation steps, decrease toxicity, and improve the oral bioavailability and permeation of cell membranes by the nucleos(t)ide analog. Prodrugs of nucleos(t)ide analogs have become the backbone of single-drug and combination-drug therapies to treat life threatening viral infections, including HIV, HBV, and HCV.

Bemnifosbuvir

Bemnifosbuvir is an investigational, novel, proprietary, orally administered double prodrug of a guanosine nucleotide analog. More specifically, it is the hemisulfate salt of a phosphoramidate protide, AT-511, that is metabolized after multistep activation to the active 5'-triphosphate metabolite, AT-9010, which is an inhibitor of SARS-CoV-2 and HCV replication.

Our medicinal chemists designed bemnifosbuvir with the following critical elements in an effort to achieve the objectives noted below:

- specific modifications at the 6-position of the purine base, acting as a prodrug, were designed to prevent the toxic effects of other such modifications and enhance cell membrane permeability, resulting in an intermediate metabolite that maximizes formation of the triphosphate active metabolite in cells;
- the stereospecific phosphoramidate, acting as a prodrug, was designed to bypass the first rate-limiting phosphorylation enzyme in the intracellular activation pathway;
- specific modifications in the sugar moiety of the purine nucleotide scaffold, to produce potent antiviral activity with a high degree of selectivity; and
- highly specific salt form to enhance solubility and drug bioavailability.

We believe that these modifications together with the double prodrug approach may impart the following potentially advantageous characteristics and features to bemnifosbuvir:

- enhanced antiviral activity and selectivity, as well as well-established pharmacology and animal models to predict clinical activity;
- favorable safety profile;
- convenience of oral administration; and
- efficient, predictable, scalable, and reproducible manufacturing, as well as long shelf life for potential stockpiling.

Because bemnifosbuvir targets viral RNA polymerase, a highly conserved enzyme critical to viral replication and transcription, via a dual mechanism, we expect it to maintain antiviral activity against emerging variants with mutations in the spike protein which is responsible for the receptor recognition and host cell membrane fusion process. In fact, the few amino acid substitutions (Y273H, P323L, and G671S) in the polymerase that emerged in past and present VOCs are all remote from the nucleoside triphosphate ("NTP") binding site and nucleos(t)ide analogs resistance sites. They belong to functionally distinct clusters providing general adaptation to the evolving virus in its human host, unlikely to confer drug resistance. Additionally, since all the enzymes involved in the metabolic pathway of bemnifosbuvir to the active triphosphate are ubiquitous host cell enzymes and not virally encoded proteins, we believe that the high rate of viral mutation does not affect the activation of bemnifosbuvir.

Development Programs

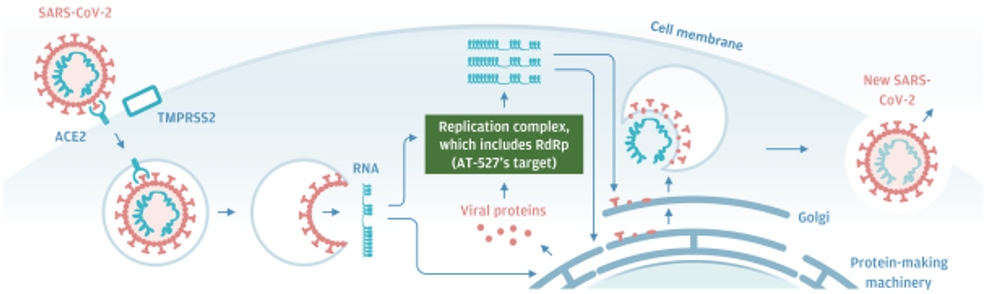
SARS-CoV-2

Background

SARS-CoV-2 is a coronavirus, belonging to the coronaviridae family, and is an enveloped virus with a positive sense ssRNA genome which encodes 29 viral proteins. It is one of six other human coronaviruses that exist, with four responsible for one third of common cold infections.

SARS-CoV-2 is structurally similar to two other life-threatening coronaviruses: SARS-CoV and Middle East Respiratory Syndrome coronavirus (“MERS-CoV-1”).

SARS-CoV-2 is a spherical virus that carries four different structural proteins: spike protein, envelope protein, membrane glycoprotein and nucleocapsid protein. As shown in the illustration below, the infection cycle begins when the spike proteins bind to the angiotensin-converting enzyme 2 cellular receptor (“ACE2”), on the surface of the target cells. A second cell surface protein, transmembrane serine protease 2 (“TMPRSS2”), enables the virion to enter the cell, where it releases its RNA. Some of this RNA is translated into new proteins using the host cell’s machinery—these proteins include the four structural proteins, as well as a number of Non-structural proteins (“Nsps”), that form the replication complex. Within this complex, RdRps catalyze the synthesis of the approximately 30,000-nucleotide RNA viral genome. The proteins and RNA are then assembled into a new virion in the Golgi and released through exocytosis.



COVID-19 – Disease Overview

Coronavirus disease 2019 ("COVID-19"), the disease caused by infection with SARS-CoV-2 and its variants, has given rise to a global pandemic that swept rapidly throughout the world beginning in 2020 and continues to cause infection and disease due to waning immunity and continued emergence of SARS-CoV-2 variants. As of February 15, 2023 according to the CDC, there have been more than 100 million confirmed cases reported and over 1.1 million deaths in the US alone and the WHO reported more than 754 million confirmed cases of COVID-19 and over 7 million deaths worldwide. In 2022, the CDC reported that COVID-19 was the third leading cause of death in the US after only heart disease and cancer with the majority of deaths occurring in patients aged 65 and older. Older adults and individuals who have risk factors are at a higher risk for developing more serious complications from COVID-19 leading to hospitalization and death.

Infection with SARS-CoV-2 may be asymptomatic or it may cause a wide spectrum of illness ranging from a mild upper respiratory tract infection to severe life-threatening sepsis and multiorgan failure. Commonly reported symptoms include fever, cough, shortness of breath, loss of taste or smell, sore throat, fatigue, headaches, muscle aches, and gastrointestinal ("GI") disturbance. Symptoms typically last two to three weeks, but many patients continue to experience symptoms for many weeks or develop new symptoms, which is now recognized as the post-acute COVID-19 syndrome, or Long COVID. COVID-19 affects people of all ages; however, people who are immunocompromised, elderly, or have certain underlying medical conditions (e.g., chronic heart, lung, and kidney disease; diabetes, obesity, and cancer) are at increased risk of poor outcomes.

The elderly (with or without comorbidities) and the immunocompromised at any age, are well documented to be unlikely to be able to mount an adequate immune response to the virus, and also seem to be unsuccessful in mounting an adequate antibody response even when vaccinated. Furthermore, many of these people are likely to be receiving concomitant medications which are recognized to have drug-drug interactions with ritonavir, meaning that they are contraindicated to receive nirmatrelvir/ritonavir. In this same population, there is considerable reluctance to use molnupiravir because of its mutagenicity and the perceived downstream consequences that may induce. With the ongoing evolution of the virus and the continual emergence of new variants, the utility of monoclonal antibodies has also been abrogated. The net result of this is that these patients currently have no access to effective outpatient therapies, are likely to need intravenous remdesivir as therapy and are also more likely to be hospitalized because of more severe disease.

While the US government has recently announced plans to end the declaration of a public health emergency associated with COVID-19, COVID-19 is expected to remain a serious endemic threat for an indefinite future period. The reasons contributing to the likelihood of COVID-19 remaining an endemic threat, include (1) viral transmission before symptom onset; (2) uneven global rollout of vaccinations; (3) ongoing vaccine hesitancy; (4) limited duration of immunity conferred by both natural infection and vaccination; (5) limited vaccine efficacy against certain SARS-CoV-2 variants; (6) limitations of current

oral antivirals such as drug-drug interactions, safety concerns and tolerability; (7) uncertain impact of vaccines on transmission; (8) continuing evolution of the virus evading endogenous and vaccine-induced immunity; and (9) diminution of virus transmission mitigation behaviors, such as wearing masks and social distancing.

Current Approaches for Prevention and Treatment of COVID-19 and Their Limitations

At the outset of the COVID-19 pandemic, unprecedented progress was made with both vaccines and treatment options for this novel disease. Despite this progress, there remain substantial limitations to currently available vaccines and therapies, including waning immunity to both naturally acquired and vaccine generated immunity, failure of certain populations to mount an adequate immune response to vaccines and lack of efficacy of currently available monoclonal antibodies to currently circulating SARS-CoV-2 subvariants (which have increased transmissibility and the ability to evade neutralizing antibodies). Limitations of current oral antivirals include DDIs with commonly prescribed medications such as seizure medications, anti-psychotics, anti-coagulants and more, and safety concerns.

As a result, there remains a continued urgent need to develop novel, safe, efficacious, convenient, oral, therapies with low risk of drug-drug interaction for the treatment of COVID-19 that can be utilized as monotherapy and potentially as part of a combination therapy. We believe that oral therapies protecting against the development of severe infection and transmission remain urgently needed particularly for vulnerable patients who currently have limited treatment options. This includes patients who are unvaccinated, patients who fail to respond to available vaccines, vaccinated patients with waning efficacy, which can occur between three to six months after immunization, and patients for whom vaccines and existing treatments are contraindicated. As COVID-19 becomes endemic with the potential for continued variant fueled pandemic surges, we believe that this need will continue for years.

Vaccines for Prevention

Several vaccines are either approved or authorized under an emergency use authorization ("EUA") and additional vaccines are in development to prevent COVID-19 infection. Approved and authorized vaccines include, among others, mRNA vaccines such as Pfizer/BioNTech's Comirnaty and Moderna's mRNA-1273, each monovalent vaccines which, were approved for the prevention of symptomatic COVID-19 caused by the original strain. These vaccines have been available in the US and globally since December 2020. More recently, in August 2022, bivalent mRNA vaccines from each of Pfizer/BioNTech and Moderna were authorized by the FDA for the prevention of symptomatic COVID-19 caused by the Omicron subvariants BA.4 or BA.5.

The ability of vaccines to produce durable immunity protection against disease and transmission is currently limited due to multiple factors, including:

- *Limited efficacy against certain viral variants.* While COVID-19 vaccines have demonstrated meaningful efficacy in preventing infection by the original strain of COVID-19, evidence shows significantly lower levels of protection against variants. Multiple clinical and real-world studies have demonstrated reduced vaccine effectiveness against the Omicron variants and subvariants.

- *Limited durability of response impacting the ability to achieve long term immunity.* Due to a combination of waning antibody titers over time, the emergence of SARS-CoV-2 variants that display significantly reduced susceptibility to vaccine and infection-induced antibodies, and the limited level of mucosal immunity conferred by systemically administered vaccines, protection against symptomatic COVID-19 is relatively short-lived. As long as significant numbers of people globally are not protected against infection and transmission, SARS-CoV-2 variants will continue to circulate and cause disease.

- *Failure of certain patient populations to mount immune response to vaccines.* The elderly (with or without comorbidities) and the immunocompromised at any age, are well documented to be unlikely to be able to mount an adequate immune response to the virus, and may also be unsuccessful in mounting an adequate antibody response even when vaccinated. The levels of pre-existing antibodies in transplant patients who had been vaccinated at least twice and

received boosters, but who required hospitalization for severe COVID-19 infection were found to be undetectable.

- *Delayed onset of protection.* The peak neutralizing antibody response conferred by currently available vaccines is usually 10 to 14 days after the final dose or booster vaccination, resulting in a period of time during which an individual is susceptible to SARS-CoV-2 infection and COVID-19 disease, despite having received the vaccine. Furthermore, given that certain vaccines require two doses, three to four weeks apart, full protection may not be achieved for several weeks after the initial dose.

- *Vaccine hesitancy.* Numerous surveys attribute vaccine hesitancy to a constellation of perceived safety, side effect and quality concerns. As of February 15, 2023, according to the CDC, only 69% of the total US population has completed the primary series of vaccines and only 16.0% have received the latest (bivalent) booster. Globally, vaccine adoption and hesitancy are generally consistent with the US figures.

Monoclonal Antibodies ("mAbs") for the treatment of COVID-19

Starting in November 2020 and into 2022, the FDA granted EUAs to several mAbs for the prophylaxis and/or treatment of COVID-19. However, the use of mAbs for the treatment of COVID-19 has been limited and is currently not authorized in the US for the following reasons:

- *Limited or no efficacy against currently circulating variants has led to the recission of all previously granted EUAs.* The clinical utility of mAbs has varied over time due to the emergence of SARS-CoV-2 variants demonstrating partial or full resistance to neutralization. Currently, in the US, with the recent revocation of the Evusheld™ EUA, the authorizations for all mAbs have been rescinded due to the high frequency of circulating SARS--CoV-2 variants that are able to evade the available neutralizing antibodies. Even if future mAbs are developed, the continued emergence of new SARS-CoV-2 variants may make even these new mAbs ineffective for the treatment of COVID-19.

- *Inconvenience of administration*. All mAbs that were previously authorized for the treatment of COVID-19 were administered intravenously. This required specialized facilities that were properly equipped to accommodate IV infusions in actively infected patients.

Antivirals for the treatment of COVID-19

Antiviral therapies, which are complementary to vaccines, have been approved or authorized for the treatment of COVID-19. In the US, Veklury® (remdesivir), an RdRp inhibitor, is approved for the treatment of COVID-19 including the treatment of outpatients at high risk of progression to severe COVID-19. Additionally, each of Lagevrio™ (molnupiravir), an orally administered direct-acting antiviral for the treatment of adults with mild to moderate COVID-19 in the outpatient setting, and Paxlovid™ (ritonavir boosted nirmatrelvir), an orally administered protease inhibitor for the treatment of adults with mild to moderate COVID-19 in the outpatient setting are authorized for use under an EUA in the US and many additional countries globally.

Limitations of currently authorized or approved antiviral therapies include:

- *Drug-Drug interactions.* Due to the potentially serious drug-drug interactions associated with Paxlovid (ritonavir-boosted nirmatrelvir) and many commonly prescribed medications, including strong CYP3A4 inducers and certain other anti-coagulant, anti-convulsant, anti-arrhythmic, chemotherapeutic, and neuropsychiatric medications, many patients with COVID-19 may be ineligible for treatment with Paxlovid or if eligible, require careful management including close monitoring of the patient by the prescriber.

- *Safety.* Lagevrio (molnupiravir) is a mutagenic ribonucleoside agent that is recommended by the NIH COVID-19 Treatment Guidelines Panel (“NIH Panel”) for use only when Paxlovid is not available, not feasible to use or clinically inappropriate. Additionally, the NIH Panel

recommends against the use of Lagevrio in pregnant patients unless there are no other options and COVID-19 therapy is clearly indicated.

- *IV infusion.* Veklury is administered via IV infusion which minimizes the convenience of administration.

Our COVID-19 strategy

We are developing bemnifosbuvir, an investigational, orally administered, novel antiviral product candidate, for the treatment of COVID-19.

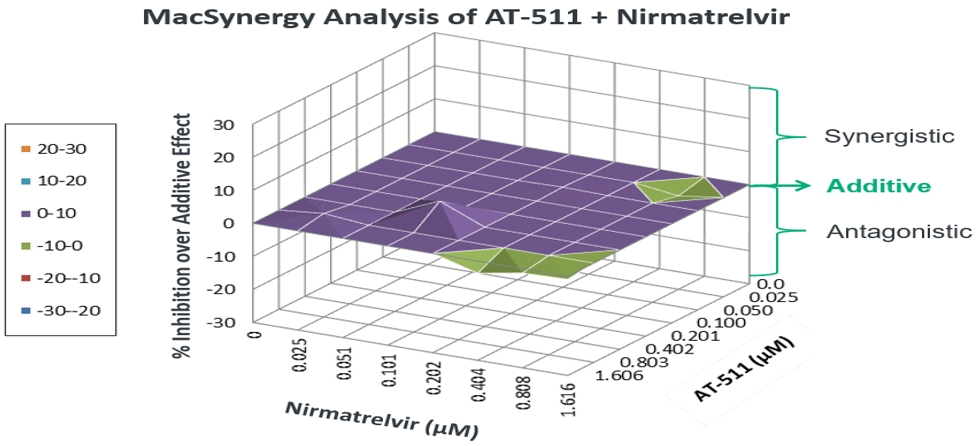
Data from the Phase 3 MORNINGSKY clinical trial that was closed out early did not meet the primary endpoint of time to symptom alleviation but the results demonstrated a 71% reduction in hospitalization (2.9% versus 10%) (p=0.047, unadjusted, exploratory; secondary endpoint) in the bemnifosbuvir arm (n=137) versus placebo (n=70). The patients enrolled in the MORNINGSKY trial consisted of a broad outpatient population including 47% who were high risk, 28% who were vaccinated, and 56% who were seropositive at baseline. In a subgroup analysis in patients greater than 40 years old, the reduction in hospitalization in the bemnifosbuvir arm of the MORNINGSKY trial was even greater at 82%. There was also a trend for clinical benefit (all-cause mortality) observed in the global phase 2 study in hospitalized patients. Although low background rates of disease progression precluded completion of the study as initially designed, all three deaths in the study occurred in placebo recipients compared to no deaths in patients receiving bemnifosbuvir. Additionally, bemnifosbuvir has demonstrated low risk of DDIs in five phase 1 clinical studies, antiviral activity against all tested VOC in *in vitro* studies, no mutagenicity or teratogenicity in *in vitro* studies and, given its mechanism of action, a high barrier to resistance.

We believe bemnifosbuvir as monotherapy has the potential to address the key limitations of current therapies and the continued unmet medical need particularly for high risk patients with limited treatment options. We have initiated SUNRISE-3, a global Phase 3 randomized, double-blind, placebo-controlled clinical trial evaluating bemnifosbuvir (550 mg BID for 5 days) in at least 1500 high-risk non-hospitalized patients with mild or moderate COVID-19.

While SUNRISE-3 is principally designed to evaluate bemnifosbuvir as monotherapy (primary analysis) it is also designed to explore of the effect of combination therapy in a smaller sub-set of patients who receive a compatible antiviral drug along with bemnifosbuvir (secondary analysis). We intend to use data from the smaller subset of patients who receive combination therapy to inform our development plans to evaluate bemnifosbuvir as combination therapy for the treatment of COVID-19.

In parallel with conducting SUNRISE-3, we are also advancing an internal discovery program focused on identifying a second generation protease inhibitor that we may potentially combine with bemnifosbuvir for combination treatment of COVID-19. We are seeking to discover a protease inhibitor that is highly potent and well tolerated with limited DDIs and does not require a Pharmacokinetic ("PK") booster (e.g., ritonavir). The optimization of lead compounds is ongoing with a target of late 2023 to submit an IND for the selected clinical candidate.

Our rationale for advancing this potential combination is based upon both historical precedents for treating serious viral diseases with combination treatments that include agents with different mechanisms of action targeting different points in the viral replication cycle and the results from the *in vitro* study we have conducted in an HCoV-229E surrogate model. In this *in vitro* study, we evaluated the antiviral activity of AT-511, the free base of bemnifosbuvir in combination with the protease inhibitor, nirmatrelvir, and the results showed an additive antiviral effect.

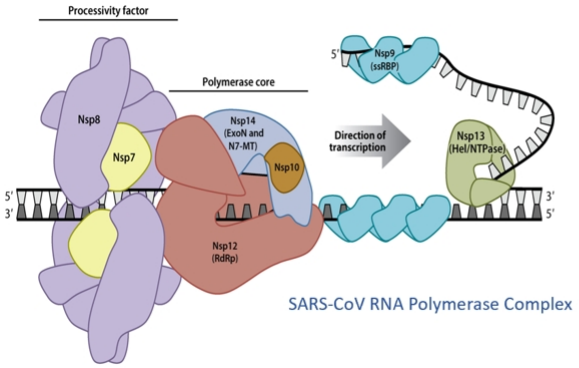


Virus: HCoV-229E
Cell: Huh7.5
Read-out: viral RNA by RT-qPCR

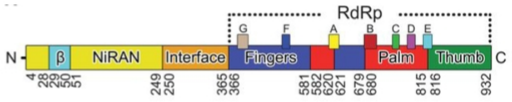
We believe these data suggest a potential benefit of the combination of bemnifosbuvir and a protease inhibitor for the treatment of SARS-CoV-2 infection.

Targeting SARS-COV-2 NiRAN/RdRp to treat COVID-19

The RNA polymerase complex of SARS-CoV and SARS-CoV-2 supports the transcription and replication of their approximately 30,000-nucleotide viral RNA genomes. It is the largest and most complex RNA synthesis machinery among RNA viruses. As shown in the illustration below, the multi-subunit SARS-CoV polymerase complex is composed of a number of Nsps including viral RdRp ("Nsp12"), processivity factors ("Nsp7", "Nsp8"), a proofreading exonuclease, a N7-methyl transferase ("Nsp14"), and a helicase ("Nsp13"). The Nsp12 protein contains two domains, a RdRp core, which is the catalytic subunit incorporating ribonucleotides into RNA templates, and an N-terminal NiRAN domain, the function of which was previously unknown.



SARS-CoV RNA Polymerase Complex



RdRp: RNA-dependent RNA polymerase
NIRAN: Nidovirus RdRp-Associated
Nucleotidyltransferase Domain

SARS-CoV RNA Polymerase

We have investigated the mechanism by which SARS-CoV initiates viral RNA synthesis and have discovered that there are two distinct pathways: one protein-primed and mediated by the NiRAN through the UMPylation of Nsp8, and the other through de novo synthesis of dinucleotide primers in a NiRAN-independent manner. Importantly, both functions can be inhibited by AT-9010, the active triphosphate metabolite of bemnifosbuvir. Furthermore, we have obtained a 2.98 Å cryo-EM quaternary structure of Nsp12/7/8/RNA/AT-9100, which confirms that AT-9010 not only bound to the NiRAN active site but also was incorporated by the RdRp and functions as a chain terminator. We believe this unique dual

mechanism of bemnifosbuvir creates a potentially higher barrier to resistance compared to other direct acting antiviral inhibitors.

Since bemnifosbuvir targets viral RNA polymerase, a highly conserved enzyme critical to viral replication and transcription, we expect it will maintain its antiviral activity even against the recently emerged variants with mutations in the spike (S) protein responsible for the receptor recognition and host cell membrane fusion process. Current COVID-19 variants have lessened the effectiveness of vaccines and eliminated the effectiveness of monoclonal antibodies due to the mutations in the viral spike protein. It is expected that future variants may also impact the effectiveness of vaccines and monoclonal antibodies.

Potent In vitro inhibition of SARS-CoV-2 replication across variants

We have assessed the *in vitro* potency of AT-511 (free base of bemnifosbuvir) against SARS-CoV-2 VOC and VOI. The data from these studies are summarized in the table below showing that AT-511 maintained its potency against all major VOC and VOI tested. These data support the key mechanistic advantage of the compound, which targets the highly conserved viral RNA polymerase.

SARS-CoV-2 variant		AT-511* EC_{90}, µM (n)		Fold change (variant/USA-WA1)
Variant	Lineage	Mean	SD	
Original (USA-WA1/2020)	A	0.75 (n=2)	0.21	-
Alpha	B.1.1.7	2.15 (n=3)	0.22	2.9
Gamma	P.1	2.50 (n=3)	0.50	3.3
Epsilon	B.1.427	0.76 (n=2)	0.48	1.0
Original (USA-WA1/2020)	A	0.43 (n=2)	0.12	
Beta	B.1.351	0.80 (n=2)	0.23	1.9
Original (USA-WA1/2020)	A	1.20 (n=3)	0.37	-
Delta	B.1.617.2	1.36 (n=3)	0.34	1.1
Original (USA-WA1/2020)	A	0.58 (n=5)	0.26	-
Omicron (BA.1)	B.1.1.529	0.50 (n=3)	0.27	0.86
Original (USA-WA1/2020)	A	0.59 (n=2)	0.18	-
Omicron (BA.2)	B.1.1.529	0.54 (n=2)	0.08	0.92
Original (USA-WA1/2020)	A	0.88 (n=2)	0.15	-
Omicron (BA.4)	B.1.1.529	0.54 (n=2)	0.27	0.61
Omicron (BA.5)	B.1.1.529	0.81 (n=2)	0.20	0.92

**Determined side-by-side in the same assay*

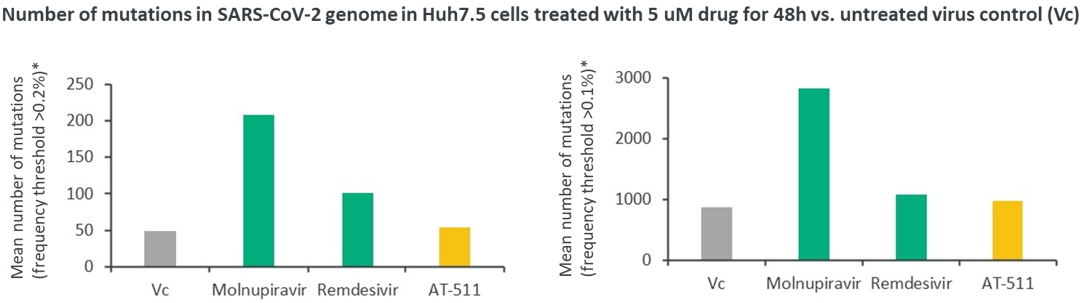
EC_{90} differences between variants were within in vitro assay variations

***No new mutation in RNA polymerase of Omicron as compared with other variants*

Non-mutagenic

Results from non-clinical studies indicated that bemnifosbuvir was non-mutagenic and non-teratogenic and it has shown no reproductive toxicity.

More specifically, analysis of SARS-CoV-2 infected Huh7.5 cells treated with AT-511 (the free base of bemnifosbuvir) by next generation sequencing ("NGS") showed that bemnifosbuvir was not a mutagen (which is consistent with the lack of genotoxicity observed in the preclinical *in vitro* and *in vivo* studies) and did not introduce mutations in the viral genome.



*Frequency threshold defined as presence of mutation in 0.2% or 0.1% of NGS reads

In addition to the standard battery of preclinical safety, pharmacology and repeat dose toxicity studies, which showed no adverse effects of bemnifosbuvir treatment in rats and non-human primates at respective doses up to 650 and 1000 mg/kg/day for 13 weeks, completed preclinical studies have demonstrated that bemnifosbuvir did not affect male or female fertility in treated rats, did not affect early embryo-fetal development in treated pregnant rats or rabbits, and did not affect the pre- or post-natal development, reproductive capability, or behavioral assessments of the offspring of rats treated prior to and during mating (males) and prior to mating through pregnancy and lactation (females).

Clinical development history

Summary

At the outset of the COVID-19 pandemic, we initiated our COVID-19 program with a global Phase 2 clinical trial of bemnifosbuvir in hospitalized patients. This was followed by the initiation, together with our former collaborator, F. Hoffmann-LaRoche Ltd. and Genentech, Inc. (together, "Roche"), of MOONSONG, a Phase 2 outpatient clinical trial, MORNINGSKY, a Phase 3 outpatient clinical trial and MEADOWSPRING, a Phase 3 six-month follow-up study for patients who had been enrolled in MORNINGSKY.

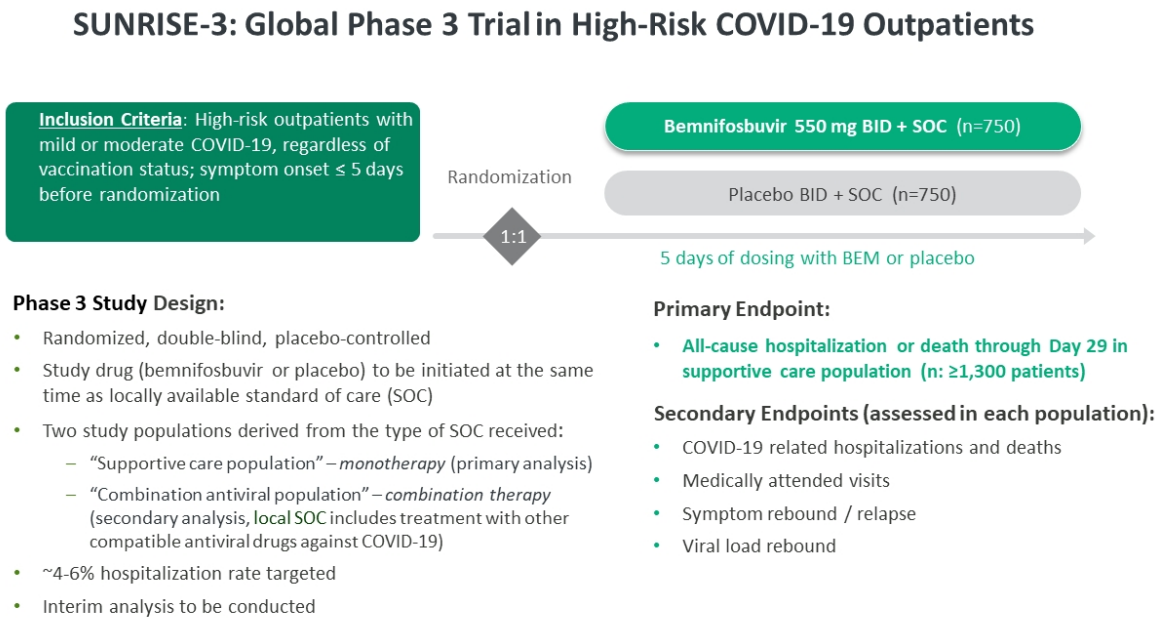
Together with Roche, we completed the Phase 2 outpatient MOONSONG clinical trial in October 2021 and with the termination of the Roche License Agreement in November 2021, we prematurely discontinued each of the Phase 3 MORNINGSKY and MEADOWSPRING clinical trials in December 2021 and March 2022, respectively. We leveraged the key clinical data obtained from these patient studies, including clinical efficacy data from MORNINGSKY, with additional supporting Phase 1 and clinical pharmacology studies conducted in healthy subjects, to support the design of the SUNRISE-3 Phase 3 clinical trial of bemnifosbuvir for the treatment of COVID-19.

SUNRISE-3 – Global Phase 3 clinical trial

SUNRISE-3 is a global, multicenter, randomized, double-blind, placebo-controlled Phase 3 clinical trial evaluating bemnifosbuvir (550 mg BID for 5 days) in at least 1,500 high-risk non-hospitalized patients with mild or moderate COVID-19. The trial will be conducted at clinical trial sites in the US, Europe, Japan, and other regions of the world. The patient population will consist of those at the highest risk for disease progression, including patients ≥ 80 years old, patients ≥ 65 years old with one or more major risk factors, and immunocompromised patients ≥ 18 years old, all regardless of COVID-19 vaccination status.

The trial is designed to evaluate bemnifosbuvir as monotherapy (primary analysis) but will also explore the impact of combination therapy in a smaller sub-set of patients who receive a compatible antiviral drug along with bemnifosbuvir (secondary analysis). The trial will include two populations derived from the type of standard of care received 1) "supportive care population" (patients who do not qualify for an approved antiviral treatment or where antivirals are not locally available) which will assess bemnifosbuvir given as monotherapy (primary analysis) and 2) "combination antiviral population" which will assess combination therapy if the SOC includes treatment with other compatible antiviral drugs against COVID-19 (secondary analysis). Patients are being randomized 1:1 to receive either bemnifosbuvir 550 mg twice-daily plus locally available SOC or placebo BID plus locally available SOC for five days.

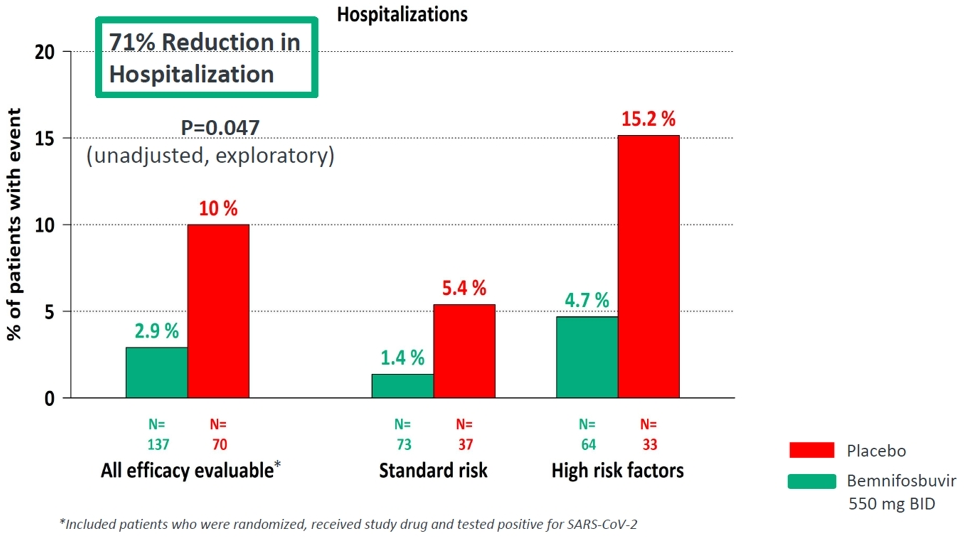
The primary endpoint of the SUNRISE-3 study is all-cause hospitalization or death through Day 29 in at least 1,300 patients in the supportive care population and is powered to detect a clinically meaningful reduction in hospitalization/death versus placebo in this population. By enriching the patients enrolling in the trial with those who are at the highest risk for disease progression, we are targeting rates of hospitalization/death of ~4-6%. An interim analysis will be conducted by a DSMB after 60% patient enrollment in the arm of the study enrolling the supportive care population. Secondary endpoints in each of the supportive care patient population and the combination antiviral population include COVID-19 complications, medically attended visits, symptom rebound/relapse and viral load rebound.



MORNINGSKY - Global Phase 3 trial

The Phase 3 MORNINGSKY study was a randomized, placebo-controlled study in non-hospitalized adult and adolescent patients with mild or moderate COVID-19 who were at high risk or standard risk for disease progression regardless of vaccination. The study, which was initiated in collaboration with Roche, was discontinued in December 2021 prior to completion as a result of the termination of the collaboration with Roche. Patients were randomized (2:1) to receive 550 mg BID bemnifosbuvir or placebo for five days. The primary endpoint was time to alleviation/improvement of COVID-19 symptoms. Secondary endpoints included hospitalization, all-cause mortality, and change in viral load. At the time of discontinuation, 216 patients had been randomized (2:1; active:placebo), with 207 patients who comprised the efficacy evaluable population. The study enrolled a broad outpatient population, including 47% who were high risk, 28% who were vaccinated, and 56% who were seropositive at baseline. Because the study was prematurely discontinued, no formal statistical comparisons were made.

While the primary endpoint of the MORNINGSKY study, time to symptom alleviation, was not achieved, the results from MORNINGSKY demonstrated a 71% reduction in hospitalization (2.9% versus 10%) (p=0.047, unadjusted, exploratory; secondary endpoint) in the bemnifosbuvir arm (n=137) versus placebo (n=70). In a subgroup analysis in patients greater than 40 years old, the reduction in hospitalization in the bemnifosbuvir arm of the MORNINGSKY trial was even greater at 82%.



There were no deaths in the study. There was no meaningful difference in the change from baseline in viral load between the bemnifosbuvir arm and the placebo arm. The 550 mg BID dose was generally well tolerated compared to placebo. There were no drug-related SAEs reported, and proportions of patients with adverse events leading to study drug discontinuation were low (2.8% in the bemnifosbuvir arm vs 7.0% in the placebo arm).

The MEADOWSPRING trial, originally designed as a six-month follow-up study of patients previously enrolled in MORNINGSKY, was also closed out in March 2022 after enrolling only 72 patients that had taken part in MORNINGSKY, a smaller number of patients than planned. As a result, firm conclusions about the long-term symptoms of COVID-19 could not be drawn from this study.

Global Phase 2 study in hospitalized patients with COVID-19

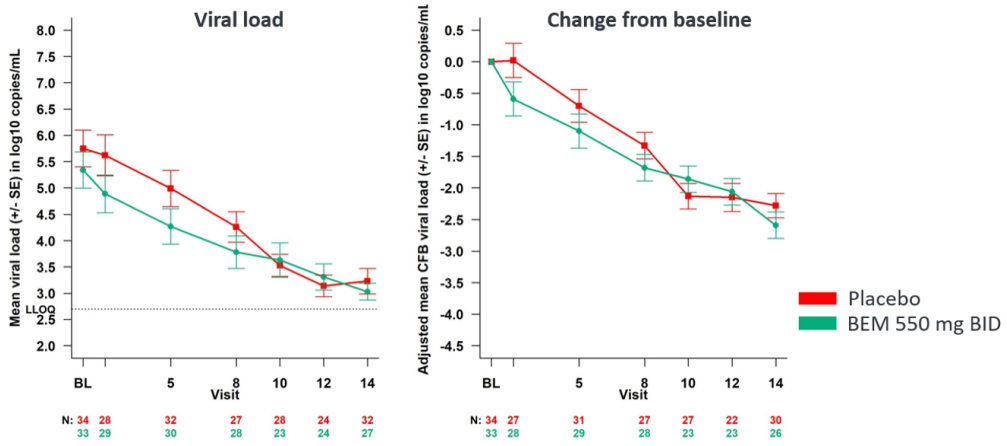
This study was a randomized, double-blind, placebo-controlled, study that evaluated bemnifosbuvir in hospitalized/confined patients with moderate COVID-19 versus placebo. The study was initially designed to assess the impact of bemnifosbuvir (550 mg BID; Part A) on Progressive Respiratory Insufficiency (PRI), however, low background rates of disease progression precluded completion of the study as initially designed. The protocol was amended to explore higher doses of bemnifosbuvir (1100 mg BID; Part B), however the study was prematurely discontinued in January 2022 due to the changing COVID-19 treatment landscape. Only two subjects (both receiving placebo) had been enrolled in Part B.

Rates for reduction of PRI were low in 550 mg BID patients and no difference was seen between treatment groups (Intent To Treat [ITT] population: 3/41 7.3% bemnifosbuvir patients and 4/40 10.0% placebo patients). The all-cause mortality for the Part A 550 mg BID subjects was 0/41 in the bemnifosbuvir group and 5.0% (2/40) in the placebo group. In addition, one placebo patient in the Part B 1100 mg BID group died.

After bemnifosbuvir 550 mg BID dosing for five days, rapid reduction in viral load levels were observed. At Day 2, patients receiving bemnifosbuvir experienced a 0.6 $\log_{10}$ greater mean reduction from baseline viral load versus placebo. A sustained difference in viral load reduction was maintained through Day 8.

Virology Results from Phase 2 Hospitalized Study in High-Risk Patients

All mITT subjects (Final analysis Part A, secondary endpoint, exploratory)



mITT = modified intent to treat analysis set; subjects who received treatment and were positive SARS-CoV-2 by central test.

Bemnifosbuvir's SARS-CoV-2 antiviral activity was also observed in patients with baseline viral loads above the median of 5.35log$_{10}$ as compared to placebo. In this subset, those in the bemnifosbuvir arm achieved SARS-CoV-2 clearance as early as Day 2 (in 6% of patients), Day 8 (in 12% of patients) Day 10 (in 33% of patients), and Day 12 (in 31% of patients) compared to 0% of patients in the placebo arm at the same timepoints. By Day 14 (last viral sampling study day) 50% of patients in the bemnifosbuvir arm and 23% in the placebo arm had no detectable RNA virus.

After dosing with 550 mg BID for five days, bemnifosbuvir was generally well tolerated and there were no drug-related serious adverse events. Non-serious adverse events were equally distributed across treatment arms. Most were mild-to-moderate in severity and assessed as not related to bemnifosbuvir.

MOONSONG - Global Phase 2 trial

This study was a randomized, double-blind, multi-center, placebo-controlled trial, that evaluated the antiviral activity, safety and pharmacokinetics of sequential doses of bemnifosbuvir 550 mg (Cohort A, n=30) and 1,100 mg (Cohort B, n=30) with BID dosing in adult outpatients with mild or moderate COVID-19 versus placebo (n=40). Treatment with bemnifosbuvir in this study did not meet the primary endpoint of showing a reduction in SARS-CoV-2 viral load in the overall population of patients compared to placebo, of whom approximately two thirds were low-risk with mild symptoms. However, in high-risk patients with underlying health conditions, a reduction of viral load of approximately 0.5 log$_{10}$ at Day 7 was observed with administration of 550 mg BID as compared to placebo (prespecified subgroup analysis Cohort A n=7; placebo n=10) and with administration of 1,100 mg BID as compared to pooled placebo (exploratory subgroup analysis Cohort B; n=14; placebo n=7).

Bemnifosbuvir was generally well tolerated in this study. The proportion of patients experiencing any adverse event ("AE") was 28% in the placebo group, 20% in the bemnifosbuvir 550 mg BID group and 33% in the bemnifosbuvir 1100 mg BID group. There were three non-drug related serious adverse events ("SAEs") in each of the treatment groups and all other AEs were grade 1 or 2. Gastrointestinal (GI)-related AEs were the most commonly reported AEs: 8% in the placebo group; 7% in the bemnifosbuvir 550 mg BID group; 20% in the bemnifosbuvir 1100 mg BID group, with mild to moderate nausea/vomiting resulting in premature study drug discontinuation of 3% in the placebo group, 0% in the bemnifosbuvir 550 mg BID group and 17% in the bemnifosbuvir 1100 mg BID group. No clinically significant differences in laboratory abnormalities were observed in the treatment arms as compared to placebo.

Other Studies

In addition to the MORNINGSKY Phase 3 clinical trial and the Phase 2 clinical trials, supporting Phase 1 and clinical pharmacology studies, including a bronchoalveolar lavage study, multiple DDI studies and a mass balance study, have been conducted and completed since we initiated our COVID-19 program. In these studies, the safety and PK of bemnifosbuvir has been evaluated at doses up to 1100 mg BID for 5 days in healthy subjects.
Results from the bronchoalveolar lavage study in healthy subjects demonstrated that bemnifosbuvir was efficiently delivered to the lungs (epithelial lining fluid), the primary site of SARS-CoV-2 infection. Five clinical DDI studies were completed with topline results demonstrating an overall low DDI potential associated with bemnifosbuvir.

Phase 1 - DDI Studies

A series of Phase 1 studies suggest a favorable drug-interaction profile, including no dosage adjustment needed for co-administration of bemnifosbuvir with drugs that are CYP3A substrates or for drugs that are sensitive substrates of efflux and hepatic uptake transporters. CYP3A is an enzyme that metabolizes many classes of medicines and supplements, and the transporters regulate cellular trafficking of drugs that are commonly prescribed among high-risk COVID-19 patients.

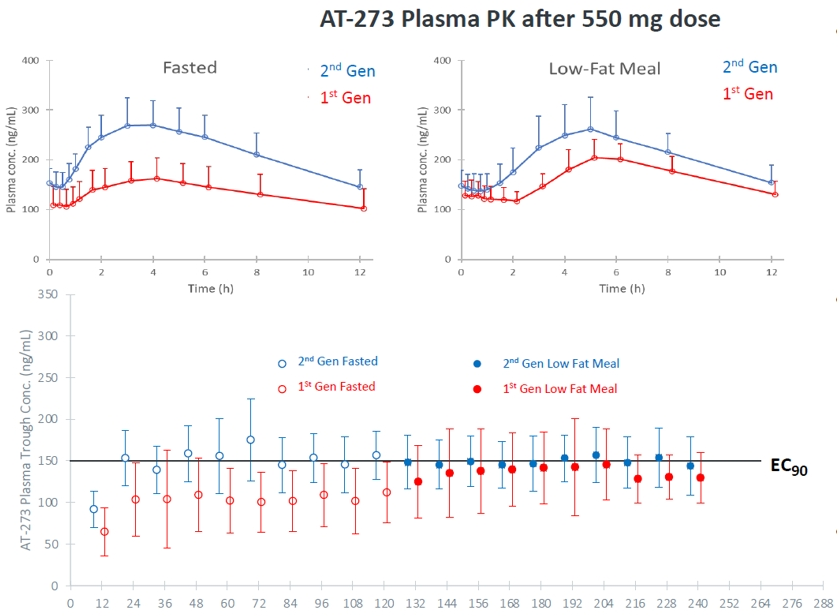
In these studies, bemnifosbuvir was administered with index drugs for CYP3A4 (midazolam), P-glycoprotein (digoxin, cyclosporine, carbamazepine), breast cancer resistance protein and organic anion transporter polypeptide 1B1 (rosuvastatin). Based on low potential for drug interaction, we believe bemnifosbuvir may be co-administered with commonly prescribed therapeutics that are often taken for other conditions by vulnerable patient populations who are at high risk for disease progression to severe COVID-19.

Bemnifosbuvir has been generally well tolerated in healthy subjects. Consistent with the results from the MOONSONG Phase 2 outpatient clinical trial, an increased incidence of mild to moderate GI-related adverse events, specifically nausea and vomiting, were observed at doses greater than 550 mg BID in healthy subjects. As 550 mg BID has been well tolerated for up to ten days, the 550 mg BID dose for five days was selected for the Phase 3 SUNRISE-3 study.

In addition, supporting clinical pharmacology studies in special populations (e.g., subjects with hepatic and renal impairment) are ongoing.

Phase 1 - PK Study – Second-generation bemnifosbuvir tablet

In the SUNRISE-3 clinical trial, we are using a second-generation formulation 275 mg tablet of bemnifosbuvir. We have evaluated this formulation in a Phase 1 study in healthy subjects who were administered bemnifosbuvir (fasted and with a low-fat meal) for ten days at 550 mg BID (2 x 275 mg). The results of this study demonstrated that the second-generation tablet had higher plasma exposures of AT-273, the active surrogate metabolite of bemnifosbuvir, than the plasma exposures obtained with the first-generation tablet which was used in the MORNINGSKY study. Additionally, the second-generation tablet achieved higher plasma trough concentrations of AT-273 (> EC_{90} of bemnifosbuvir in inhibiting SARS-CoV-2 replication) without food effect and regardless of fat content. In this study, bemnifosbuvir was generally well-tolerated in healthy subjects.



Bemnifosbuvir and Ruzasvir for the Treatment of Hepatitis C

Hepatitis C virus (HCV)

Background

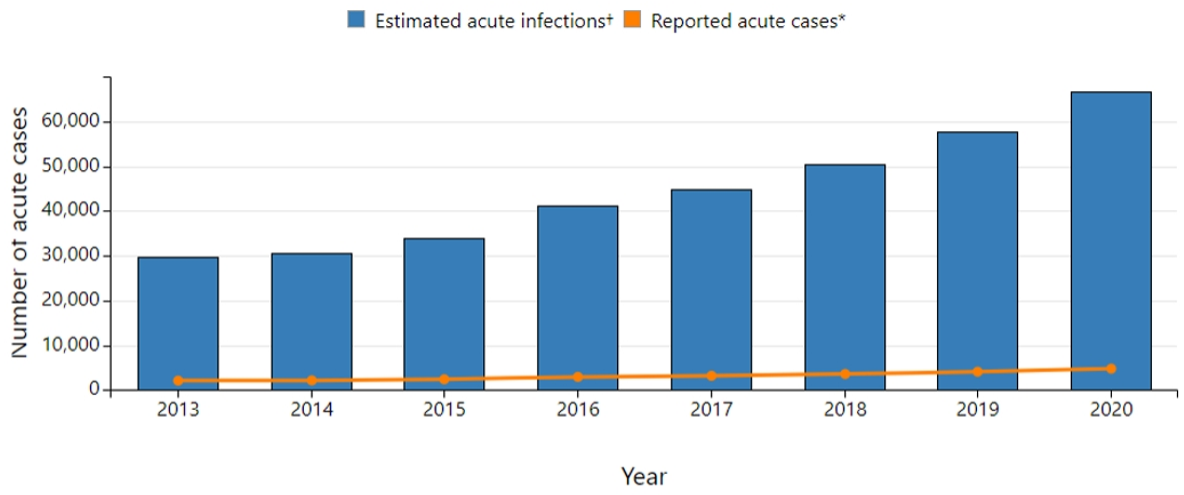
HCV is a blood-borne, positive sense, ssRNA virus, primarily infecting cells of the liver. HCV is a leading cause of chronic liver disease and liver transplants and spreads via blood transfusion, hemodialysis, and needle sticks. In the US, injection drug use accounts for approximately 60% of all new cases of HCV. Diagnosis of HCV is made through blood tests, including molecular tests that allow for the detection, quantification and analysis of viral genomes and the classification of an infection into specific viral genotypes. Hepatitis C becomes chronic Hepatitis C in 75% to 85% of acute cases, with an incubation period lasting from two to 26 weeks.

HCV is classified into seven genotypes and 67 subtypes, with genotype 1 being responsible for more than 70% of HCV cases in the US. Patients with HCV are also classified by liver function status: compensated cirrhosis (liver scarring) denotes those patients that do not yet have impaired liver function, while decompensated cirrhosis describes patients with moderate to severe liver function impairment.

According to the WHO, an estimated 58 million people globally have chronic HCV infection, with about 1.5 million new infections occurring per year. The most recently published CDC HCV surveillance report showed a continuing increase in HCV infections in the US. Approximately 290,000 people die every year from HCV related liver diseases, with the majority of deaths related to cirrhosis and hepatocellular carcinoma.

The incidence rate of acute HCV has more than doubled since 2013 (124% increase). However, there is a wide gap between the number of reported cases versus estimated cases. Most individuals who become infected with HCV remain unaware that they are infected because HCV can go undetected until the condition progresses to symptomatic disease or until specific clinical tests are performed to confirm diagnosis. Consequently, cases are unreported, skewing actual disease prevalence rates. The burden of underreporting is realized when high medical expenditures (comorbid treatment costs, liver transplants) and mortality rates from advanced chronic liver disease do not proportionally align with reported prevalence rates.

Increasing Incidence of HCV in the US



Source: Centers for Disease Control and Prevention (CDC). 2020 Viral Hepatitis Surveillance Report—Hepatitis C. Published September 2022.

Despite significant advances in treatment beginning in 2013, there remains a large, underserved, HCV patient population which continues to grow dramatically in the US. While a portion of this rise in incidence results from increased diagnosis of HCV that began following the 2013 CDC issuance of guidelines for screening of all Americans born between the years 1945 and 1965, a large portion of this increase in incidence is attributable to the opioid crisis, IV drug use and HCV reinfection.

The US HCV prevalence is expected to continue to remain steady over the coming years as rising HCV incidence offsets the number of new patients treated. It is estimated that a substantial global market for HCV therapeutics will exist to 2050 and beyond. Estimated at approaching $4 billion in global sales in 2022, with approximately 50% attributable to the US, the HCV market remains large.

Current treatment landscape

No vaccine exists for the prevention of HCV, but beginning in 2013 several sequentially introduced and improved oral antiviral therapeutics have boosted SVR rates to over 95% in a majority of patients, with treatment durations of eight to 12 weeks depending upon the regimen and patient population. The leading HCV products are combination therapies comprised of agents with differing mechanisms of action and therapeutic targets: NS3/4A protease inhibitors, NS5A inhibitors, and NS5B nucleos(t)ide polymerase inhibitors. A patient's genotype, cirrhotic status, and prior treatment failures determine the appropriate antiviral therapeutic used in treatment. In the US, currently the two leading therapeutics for treatment of chronic HCV are:

Epclusa® (sofosbuvir/velpatasvir): a combination regimen consisting of an NS5B inhibitor and an NS5A inhibitor, was first approved by the FDA in 2016. It is indicated for the treatment of adults and pediatric patients ≥3 years with chronic HCV genotype one through six infection, either without cirrhosis or with compensated cirrhosis. For patients with decompensated cirrhosis, Epclusa is approved for use in combination with ribavirin (a purine nucleoside analog). Patients on Epclusa require 12 weeks of treatment.

Mavyret® (glecaprevir/pibrentasvir): a combination regimen consisting of a NS3/4A protease inhibitor and an NS5A inhibitor was first approved by the FDA in 2017. It is indicated for the treatment of adults and pediatric patients ≥3 years with chronic HCV genotype one through six infection, without cirrhosis or with compensated cirrhosis. Mavyret is also approved for HCV patients with genotype 1 infection who have been previously treated with a regimen either containing an NS5A inhibitor or an NS3/4A protease inhibitor (but not both). Mavyret was the first eight-week treatment approved for HCV genotypes one through six in adult patients without cirrhosis and with compensated cirrhosis who have not been

previously treated. Longer treatment durations (up to 16 weeks) are indicated for some treatment-experienced populations. Mavyret is not approved for use in patients with decompensated cirrhosis.

Our approach – seeking to improve the standard of care

We are developing bemnifosbuvir in combination with ruzasvir for the treatment of HCV. Bemnifosbuvir is a potent inhibitor of the HCV nonstructural protein 5B ("NS5B") RdRp. Ruzasvir is an investigational oral, potent, pan-genotypic nonstructural protein 5A ("NS5A") inhibitor for the treatment of chronic HCV infection that we licensed from Merck in December 2021. Based on our preclinical and clinical data to date, we believe that this combination, if approved, could offer the following potential benefits:

- Convenient and short duration (eight weeks) protease inhibitor-free treatment in HCV-infected patients with or without cirrhosis.
- Equivalent antiviral potency across all genotypes, regardless of cirrhosis status, including the difficult to treat genotype-3 population.
- Obviate the need for extensive pretreatment assessments, including genotyping, procedures to assess cirrhosis, and liver function assessment.
- Potential to be the first ribavirin-free therapy for decompensated cirrhosis. Ribavirin, an antiviral first approved in 1986, carries several FDA boxed warnings, including the risk of hemolytic anemia and teratogenicity.
- Well tolerated regimen, with low potential for drug-drug interactions.

Clinical development

To date, we have completed two clinical trials of bemnifosbuvir to support the treatment of chronic HCV infection.

Phase 1 clinical trial of bemnifosbuvir as a single agent

We conducted a Phase 1 trial to evaluate single and multiple doses of bemnifosbuvir as a single agent in healthy and HCV-infected subjects for up to seven days. All HCV-infected subjects were treatment-naïve with HCV RNA ≥5 log10 IU/mL. The objectives of the trial were to assess safety, tolerability, PK and antiviral activity.

The trial evaluated single oral doses of bemnifosbuvir up to 400 mg salt form (369 mg free base) in healthy subjects (Part A), single doses up to 600 mg salt form (553 mg free base) in non-cirrhotic HCV-infected subjects (Part B), and multiple doses up to 600 mg salt form (553 mg free base) once daily for seven days in non-cirrhotic genotype 1b (“GT1”), HCV-infected subjects (Part C). Additional cohorts evaluated 600 mg salt form (553 mg free base) once daily for seven days in non-cirrhotic genotype 3 (“GT3”), (Part D) and Child-Pugh A cirrhotic (GT 1,2,3), HCV-infected subjects (Part E). The tables below show the dosage and mean maximum HCV RNA reductions for each treatment cohort.

A total of 88 subjects were dosed across all parts of the trial, with 72 subjects who received active drug and 16 subjects who received placebo. In this trial, bemnifosbuvir showed equivalent pan-genotypic antiviral activity in both cirrhotic and non-cirrhotic HCV infected patients. The mean maximum HCV reduction after a single dose (Part B) was 2.3 $\log_{10}$ IU/mL, and the mean maximum HCV RNA reduction after seven days of dosing with bemnifosbuvir at 553 mg free base was 4.6 $\log_{10}$IU/mL. Data also showed a mean maximum HCV RNA reduction of 4.4 $\log_{10}$IU/mL after seven days of dosing of bemnifosbuvir at 553 mg free base in non-cirrhotic genotype 1b (“GT1b”), HCV-infected subjects, and a mean reduction of 4.5 $\log_{10}$ IU/mL after seven days of dosing in non-cirrhotic GT3 HCV-infected subjects. The PK data in cirrhotic subjects was similar to non-cirrhotic subjects. Emax modeling predicted that a dose of 553 mg free base of bemnifosbuvir once daily would result in maximum viral load reduction.

Maximum HCV RNA change in Part B (single dose in non-cirrhotic, GT1 HCV-infected subjects)

Maximum Reduction (log_{10} IU/mL) bemnifosbuvir dosage (free base equivalent)	100 mg (92 mg) N=3	300 mg (277 mg) N=3	400 mg (369 mg) N=3	600 mg (553 mg) N=3
Mean ±SD*	0.8 ±0.153	1.7 ±0.564	2.2 ±0.391	2.3 ±0.255
Individual	0.6, 0.8, 0.9	1.1, 1.8, 2.2	1.8, 2.2, 2.5	2.1, 2.3, 2.6

Maximum HCV RNA change in Part C (multiple dose in non-cirrhotic, GT1 HCV-infected subjects)

Maximum Reduction (log_{10} IU/mL)	Placebo QD** x 7 days (N=6)	150 mg (138 mg) QD x 7 days (N=6)	300 mg (277 mg) QD x 7 days (N=6)	600 mg (553 mg) QD x 7 days (N=6)
Mean ±SD	0.4±0.109	2.6±1.073	4.0±0.415	4.4±0.712
Individual	0.3, 0.3, 0.4, 0.4, 0.5, 0.6	1.7, 1.8, 1.8, 2.7, 3.0, 4.5	3.4, 3.7, 3.9, 4.2, 4.2, 4.5	3.5, 4.0, 4.1, 4.3, 5.2, 5.3

Maximum HCV RNA change in Part D (multiple dose in non-cirrhotic, GT3 HCV-infected subjects) and Part E (multiple dose in cirrhotic HCV-infected subjects)

Maximum Reduction (log_{10} IU/mL)	Part D – GT3	Part E – Cirrhotic
	600 mg (553 mg) QD x 7 days (N=6)	600 mg (553 mg) QD x 7 days (N=6)
Mean ±SD	4.5±0.262	4.6±0.485
Individual	4.2, 4,4, 4.4, 4.5, 4.5, 5.0	GT1b: 4.0, 4.0, 4.5 GT2: 5.0 GT3: 4.8, 5.2

* SD = standard deviation

** QD = once daily

Phase 2 clinical trial of bemnifosbuvir in combination with daclatasvir

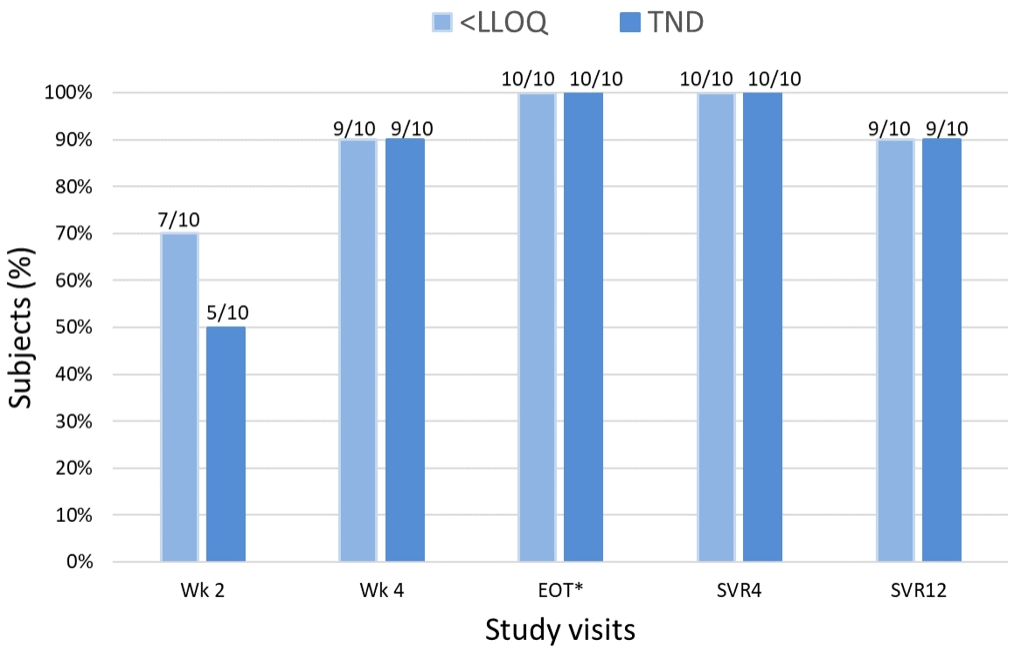
We conducted a Phase 2, open-label clinical trial to evaluate bemnifosbuvir in combination with daclatasvir, an approved commercially available HCV NS5A inhibitor, in HCV-infected subjects. Ten treatment-naïve, non-cirrhotic GT1 HCV-infected subjects received 553 mg free base bemnifosbuvir and 60 mg daclatasvir once daily for a period of eight or 12 weeks. The primary efficacy endpoint of the study was SVR12 (a sustained viral response, defined as HCV RNA < lower limit of quantitation ("LLOQ") at 12 weeks after end of treatment ("EOT")). Secondary efficacy endpoints included HCV RNA< Lower Limit Of Quantitation (“LLOQ”), and Target Not Detected (“TND”) (an assessment of virologic response that is more rigorous than LLOQ), by study visit, virologic failure, and appearance of resistance-associated variants ("RAVs") to either of the study drugs.

Despite the use of a less potent first-generation HCV NS5A inhibitor, daclatasvir, all subjects achieved HCV RNA < LLOQ and TND at the end of treatment; nine of the ten subjects achieved SVR12. One subject who was TND by week two received eight weeks of treatment, achieved SVR4, and then experienced likely virologic relapse at post-treatment week 12. The single subject who relapsed with GT 1b virus had the following multiple RAVs/variants both at baseline and at the SVR12 timepoint: NS5A: R30Q; NS5B: L159F/A218S/C316N. Phenotypic analysis demonstrated that bemnifosbuvir retained the same potency against clinical isolates obtained from this relapsed subject at baseline and SVR12 (only a 1.1 and 0.8-fold shift, respectively, in EC_{50} compared to reference). Compared to sofosbuvir, the EC_{50} and EC_{90}values for bemnifosbuvir were ~10-fold lower. Thus, the significance of the RAVs in this case is unclear. No other subjects had pre-existing NS5A RAVs at baseline.

As shown in the graph below, viral load decreased rapidly after initiation of study drugs, with 70% of subjects achieving plasma HCV RNA < LLOQ by week two (and 50% achieving TND by week 2). We believe that the rapid early clearance of HCV RNA observed in this trial supports continued evaluation of

bemnifosbuvir in shortened treatment regimens, ideally with a more potent, next-generation HCV NS5A inhibitor.

Proportion (%) of subjects achieving HCV RNA <LLOQ and TND by study visit with bemnifosbuvir in combination with daclatasvir



Bemnifosbuvir HCV safety

There were no serious adverse events, dose-limiting toxicities or adverse events leading to trial discontinuation observed in our HCV Phase 1 or Phase 2 clinical trials of bemnifosbuvir. The most common side effects observed were headache and small increases in blood lipid levels, with no consistent patterns in other reported effects. Most side effects were not severe and were not thought to be related to bemnifosbuvir.

Ruzasvir

Ruzasvir is an investigational oral, pan-genotypic NS5A inhibitor that we licensed from Merck in December 2021. In studies conducted by Merck, ruzasvir demonstrated *in vitro* potent antiviral activity with an EC_{50}in the sub- to low picomolar range against all HCV genotypes (<10 pM against GTs 1-7). The antiviral activity of ruzasvir was evaluated in a proof-of-concept ("POC") study in HCV-infected patients, where viral load reductions >3 log_{10} were observed in GT1, GT2 and GT3-infected patients after treatment with monotherapy. This clinical antiviral activity is on par with what was achieved, as single agents, with pibrentasvir and velpatasvir, the NS5A inhibitor components of Mavyret and Epclusa, respectively. These POC data supported evaluation of ruzasvir in larger phase 2 multiple drug combination studies (including two and three drug regimens) previously conducted by Merck. These studies included treatment-naïve and interferon-experienced patients with or without compensated cirrhosis. In general, high SVR12 rates (>90%) were observed in two-drug combination studies (ruzasvir plus uprifosbuvir, a pyrimidine nucleotide prodrug, for 12 weeks) conducted by Merck in GT1, GT2, GT4 and GT6-infected patients (C-Breeze 1 and 2). A lower SVR12 rate was observed in GT-3 subjects with compensated cirrhosis (40% SVR12; C-Breeze 1). We believe this lower rate is attributed to the reduced antiviral activity associated with the nucleotide uprifosbuvir in GT-3 cirrhotic subjects as an increase in ruzasvir dose to 180 mg substantially increased the SVR12 rate in this population (68% SVR12; C-Breeze 2), highlighting the preserved dose-related clinical antiviral activity of ruzasvir in GT-3 subjects with cirrhosis.

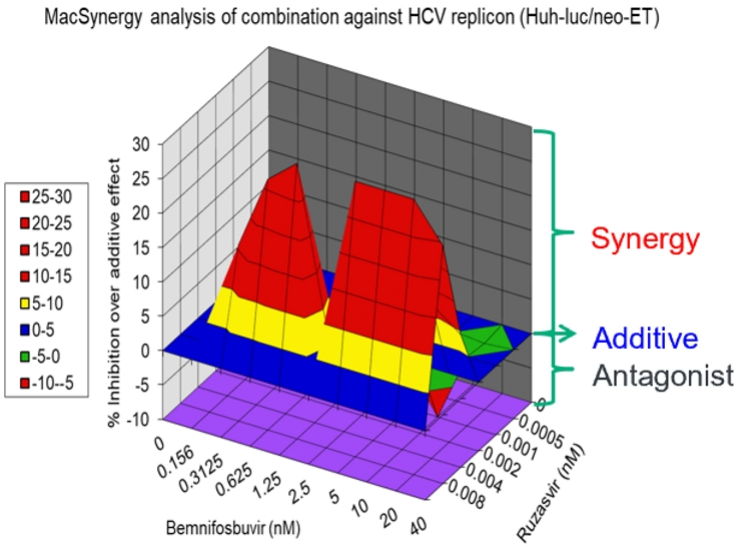
Over 1200 HCV-infected participants have received ruzasvir at daily doses up to 180 mg for durations up to 24 weeks as part of 2-drug and 3-drug regimens with or without ribavirin. The overall safety data indicates that ruzasvir has been generally well-tolerated with no consistent treatment-related changes in labs, vital signs, or ECG parameter values. Serious adverse events and discontinuations due to adverse events were rare in all studies conducted by Merck.

Rationale supporting the combination of bemnifosbuvir and ruzasvir for HCV

With the antiviral potency observed with bemnifosbuvir, especially in more difficult to treat genotype-3 infected patients, we believe that the combination of ruzasvir and bemnifosbuvir has the potential to improve on the SVR12 rates observed in the prior studies conducted by Merck.

To further support our development of the combination of bemnifosbuvir and ruzasvir in patients, we have conducted *in vitro* synergy experiments in HCV GT1b replicon assays (Huh-luc/neo-ET), where HCV replicon cells were treated with multiple concentrations of AT-511, the free base of bemnifosbuvir, and ruzasvir either alone or in combination. As shown in the figure below, these experiments demonstrated that the combination resulted in substantially greater inhibition of HCV replication than either agent alone, suggesting a synergistic antiviral effect between the two inhibitors.

In vitro Synergy: Assay performed in HCV GT1b replicon (Huh-luc/neo-ET)



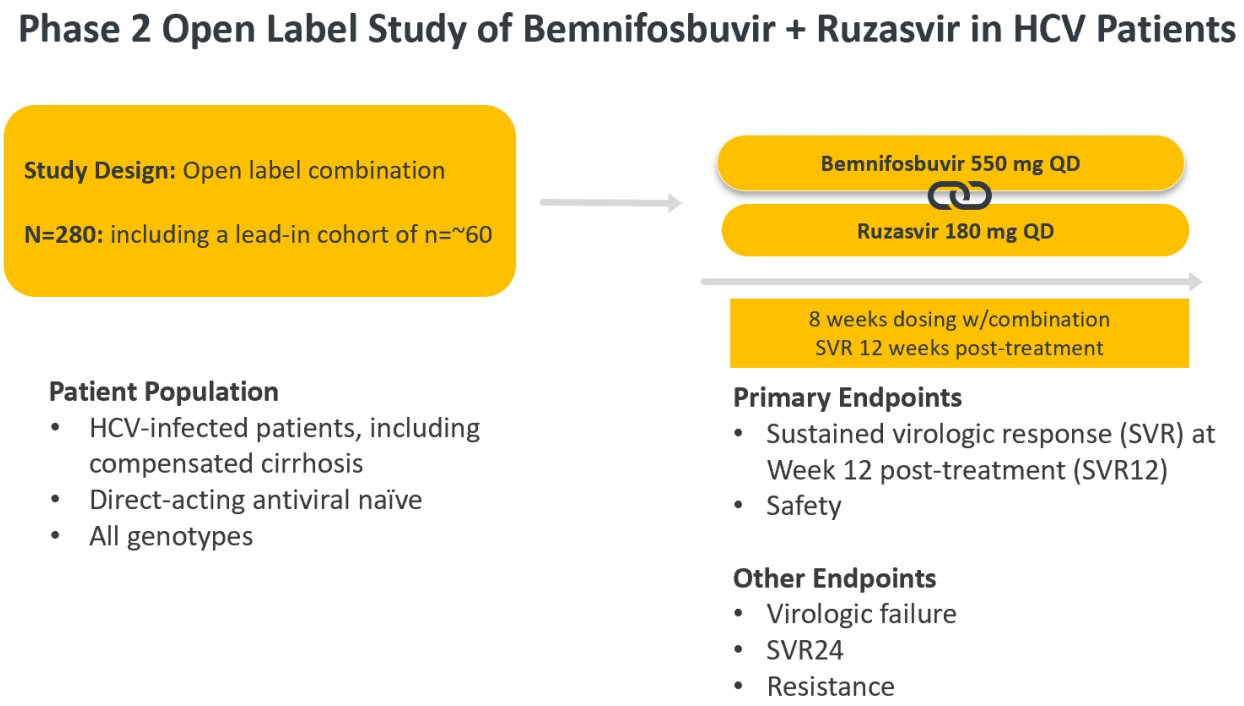
In a 13-week combination toxicity study in rats, bemnifosbuvir and ruzasvir were well tolerated when administered orally at 500 mg/kg/day alone or in combination. No test article-related adverse effects were noted for any of the three dose groups. Systemic exposures of bemnifosbuvir, its metabolites, and ruzasvir were similar when dosed alone or in combination, suggesting no significant drug-drug interactions between the two drugs.

Collectively, these data support the clinical development of bemnifosbuvir and ruzasvir used in combination for the treatment of chronic HCV infection.

Planned clinical development

In the second quarter of 2023, we plan to initiate enrollment of a Phase 2 trial of bemnifosbuvir in combination with ruzasvir in treatment-naïve, HCV-infected patients either without cirrhosis or with compensated cirrhosis. This study is designed to evaluate the safety and efficacy of the pan-genotypic combination consisting of 550 mg QD of bemnifosbuvir and 180 mg QD of ruzasvir after eight weeks of treatment. Approximately 280 HCV-infected, direct-acting antiviral naive patients across all genotypes,

including a lead-in cohort of approximately 60 patients are expected to be enrolled in this Phase 2 study. The primary endpoints of the study are safety and SVR at Week 12 post-treatment. Other virologic endpoints include virologic failure, SVR at Week 24 post-treatment and resistance.



Results from this study, if positive, may support future larger studies of bemnifosbuvir in combination with ruzasvir in broad patient populations for treatment durations of eight weeks or potentially less (six weeks) as well as in patients with decompensated cirrhosis for treatment durations of 12 weeks without ribavirin. Currently we are conducting a Phase 1 clinical study in healthy subjects to evaluate the potential DDI between bemnifosbuvir and ruzasvir and the effect of food on the PK of the agents.

Roche License Agreement

In October 2020, we entered into a License Agreement with F. Hoffmann-La Roche Ltd and Genentech, Inc. (“Roche License Agreement”) in connection with the global development, manufacture and commercialization of bemnifosbuvir, AT-511, their backup compounds (including AT-752) (“Licensed Compounds”), products containing any Licensed Compound (“Licensed Products”), and related companion diagnostics (“Companion Diagnostics”).

As partial consideration for the rights we granted to Roche under the Roche License Agreement, Roche paid us an upfront payment of $350 million in November 2020. Additionally, upon realization of a development milestone in June 2021, we received an additional $50 million from Roche.

During the term of the Roche License Agreement, Roche and we jointly developed bemnifosbuvir for COVID-19 on a worldwide-basis and equally shared the costs associated with such development activities.

On February 10, 2022, the Roche License Agreement terminated following our receipt of notice of termination from Roche in November 2021. As of the termination date, our obligations under the cost sharing arrangement with Roche associated with the development of bemnifosbuvir also ended.

As a result of the termination of the Roche License Agreement, we have regained worldwide exclusive rights from Roche to research, develop, manufacture and commercialize the Licensed Compounds, the Licensed Products and the Companion Diagnostics in all fields of use.

License Agreement with Merck

In December 2021, we entered into a license agreement with Merck ("Merck License Agreement") for the development, manufacture and commercialization of ruzasvir. Ruzasvir is the NS5A inhibitor we are developing in combination with bemnifosbuvir for the treatment of HCV.

Pursuant to the terms of the Merck License Agreement, we obtained from Merck an exclusive (subject to certain reserved rights to conduct internal research), sublicensable, and worldwide license under certain Merck patents and know-how to research, develop, manufacture, have manufactured, use, import, export, sell, offer for sale, and otherwise commercialize ruzasvir ("Compound), or products containing the Compound (each a "Product") for all therapeutic or prophylactic uses in humans ("Field").

In consideration for the rights we acquired under the Merck License Agreement, we paid Merck an upfront payment in the amount of $25 million and we will be required to pay Merck milestone payments up to $135 million in the aggregate upon our achievement of certain development and regulatory milestones and up to $300 million in the aggregate upon our achievement of certain sales based milestones. Additionally, we have agreed to pay Merck tiered royalties based on annual net sales of Products ranging from high single digit to mid teens percentages, subject to certain adjustments. Our royalty payment obligations will continue on a country-by-country and Product-by-Product basis until the later of (i) the expiration of the last to expire valid claim of a licensed Merck patent claiming such Product (or a Compound contained in such Product) and (ii) a period of years after the first commercial sale of such Product in such country.

Under the terms of the Merck License Agreement, we are obligated to use commercially reasonable efforts to develop and commercialize at least one Product in the Field in certain countries.

The term of the Merck License Agreement will continue, on a Product-by-Product and country-by-country basis, until expiration of all royalty payment obligations arising under the Merck License Agreement. We may terminate the Merck License Agreement for convenience upon 90 days prior written notice. Each party has the right to terminate the Merck License Agreement in the event of the other party's material breach of the terms of the Merck License Agreement subject to a 60 day cure period and in the event of the other party's bankruptcy or insolvency. Merck has the right to terminate the Merck License Agreement immediately if we commence any interference or opposition proceeding or other challenge to the validity or enforceability of any Merck patent licensed to us under the Merck License Agreement or if we otherwise oppose any extension of, or the grant of any supplementary protection certificate with respect to, any such Merck patent.

Upon any termination of the Merck License Agreement, the license granted to us by Merck will terminate. Upon termination of the Merck License Agreement by us for convenience other than as a result of a safety issue, or upon any termination by Merck, Merck will have an exclusive, fully paid, perpetual, sublicensable license to certain of our patents and know-how that are reasonably necessary to develop, manufacture or commercialize a Product that contains ruzasvir as the sole active agent, as such Product exists at termination. Additionally, if requested by Merck, during a period of time after delivery of the notice of termination of the Merck License Agreement by Merck or by us for convenience other than as a result of a safety issue, we will have the obligation to negotiate with Merck for the grant to Merck of a non-exclusive, royalty bearing license to certain of our patents and know-how that are reasonably necessary to develop, manufacture or commercialize a Product that is comprised of the combination of ruzasvir and bemnifosbuvir, as such Product exists at termination, with certain license terms pre-specified in the Merck License Agreement.

Manufacturing

We do not currently own or operate manufacturing facilities for the production of preclinical or clinical product candidates, nor do we have plans to develop or operate our own manufacturing operations in the future. We currently rely upon third-party contract manufacturing organizations ("CMOs") to produce our product candidates for both preclinical and clinical use. Although we rely on CMOs, we also have personnel with extensive manufacturing experience that can oversee the relationship with our manufacturing partners. We believe that any materials required for the manufacture of our product candidates could be obtained from more than one source.

Competition

As a clinical-stage biopharmaceutical company, we face competition from a wide array of companies in the pharmaceutical and biotechnology industries. These include both small companies and large companies with much greater financial and technical resources and far longer operating histories than our own. We may also compete with the intellectual property, technology, and product development efforts of academic, governmental, and private research institutions.

Our competitors may have significantly greater financial resources, established presence in the market, expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement, and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific, sales, marketing, and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors affecting the success of any product candidates that we develop, if approved, are likely to be their efficacy, safety, convenience, price, and the availability of reimbursement from government and other third-party payors. Our commercial opportunity for any of our product candidates could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours and may commercialize products more quickly than we are able to.

We are aware of the following competitors in the areas that we are currently targeting:

SARS-CoV-2

Many therapies and vaccines are approved or authorized for emergency use for the treatment and prevention, respectively of COVID-19 in the US and multiple additional countries. In addition to approved or authorized products, there are a number of other agents in development for the treatment of COVID-19.

Direct acting antiviral therapies for the treatment of COVID-19 that are currently approved or authorized for use include:

- Paxlovid™ (nirmatrelvir tablets and ritonavir tablets) (Pfizer Inc.), a protease inhibitor boosted by ritonavir authorized for emergency use by the FDA for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) at high risk for progression to severe COVID-19, including hospitalization or death.
- Lagevrio™ (molnupiravir) (Ridgeback Biotherapeutics LP/Merck & Co., Inc.), a ribonucleoside analog authorized for emergency use by the FDA for the treatment of mild-to-moderate COVID-19 in adults at high-risk for progression to severe COVID, including hospitalization or death and for whom alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate.
- Veklury® (remdesivir) (Gilead Sciences, Inc.), a nucleotide analog RdRp inhibitor approved by the FDA for the treatment of COVID-19 in adults and pediatric patients (12 years of age and older and weigh at least 40 kg) who are (i) hospitalized, or (ii) not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization and death. Additionally, the FDA has granted an emergency use authorization for the treatment of pediatric patients weighing 3.5 kg to less than 40 kg or pediatric patients less than 12 years of age weighing at least 3.5 kg who are (i) hospitalized, or (ii) not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization of death.

Other orally administered investigational agents that are currently in development for the treatment of COVID-19 include:

Investigational Therapy	Company	Mechanism of Action	Phase of Development
GS-5245	Gilead Sciences, Inc.	Nucleoside analog	Phase 3
VV116	Junshi Biosciences	Nucleoside analog	Phase 3
Ensitrelvir (S-217622)	Shionogi	Protease inhibitor	Phase 3
Simnotrelvir (SIM0417)	Jiangsu Simcere Pharmaceuticals	Protease inhibitor	Phase 2/3
EDP-235	Enanta Pharmaceuticals	Protease inhibitor	Phase 2
PBI-0451	Pardes Biosciences	Protease inhibitor	Phase 2
Pentarlandir	SyneuRx	Protease inhibitor	Phase 2

In addition to the antivirals listed above, a number of monoclonal antibodies were previously authorized for emergency use for the prophylaxis or treatment of COVID-19. While these authorizations have been currently rescinded in the US, it is possible that monoclonal antibodies which have effectiveness against future SARS-CoV-2 variants may be developed and authorized or approved for the treatment of COVID-19.

Vaccines and associated vaccine boosters that are approved or authorized for emergency use for the prevention of COVID-19 include:

- Comirnaty® (COVID-19 Vaccine, mRNA) (Pfizer-BioNTech), an FDA-approved (August 23, 2021) monovalent mRNA vaccine for the prevention of 2019 coronavirus disease (COVID-19) in individuals six months and older.
- Pfizer-BioNTech (COVID-19 Vaccine, Bivalent) (Pfizer-BioNTech), an FDA-EUA (August 2022) bivalent mRNA bivalent vaccine for the prevention of COVID-19 in individuals 12 years of age and older as a single booster dose administered at least two months after either: 1) completion of primary vaccination with any FDA authorized or approved monovalent COVID-19 vaccine, or 2) receipt of the most recent booster dose with any FDA authorized or approved monovalent COVID-19 vaccine.
- Spikevax® (COVID-19 Vaccine, mRNA) (Moderna), an FDA-approved (January 31, 2022) monovalent mRNA vaccine for the prevention of 2019 coronavirus disease (COVID-19) in individuals 6 months and older.
- Moderna (COVID-19 Vaccine, Bivalent), FDA-EUA (January 2022) bivalent mRNA vaccine, for the prevention of COVID-19 in individuals 18 years of age or older as a single booster dose administered at least 2 months after either: 1) completion of primary vaccination with any FDA authorized or approved monovalent COVID-19 vaccine, or 2) receipt of the most recent booster dose with any FDA authorized or approved monovalent COVID-19 vaccine.
- Janssen COVID-19 vaccine, FDA-EUA (February 2021) for the prevention of COVID-19 for individuals 18 years of age and older for whom other FDA-authorized or approved COVID-19 vaccines are not accessible or clinically appropriate, and in individuals 18 years of age and older who elect to receive the Janssen COVID-19 Vaccine because they would otherwise not receive a COVID-19 vaccine. Single booster doses may be administered at least 2 months after the primary vaccination or administered as a heterologous booster dose following completion of primary vaccination with another authorized or approved COVID-19 vaccine. The dosing interval for the heterologous booster dose is the same as that authorized for a booster dose of the vaccine used for primary vaccination.
- Novavax COVID-19 Vaccine, Adjuvanted, FDA-EUA (July 2022) for the prevention of COVID-19 for individuals 18 years of age and older

The potential treatments and vaccines for COVID-19 continue to evolve. The list above addresses the products or product candidates approved or authorized for emergency use or under clinical development in the US as of the date of this Annual Report on Form 10-K that we believe could be the most

competitive with a bemnifosbuvir therapy but is not a comprehensive list of every treatment that is in development for COVID-19.

HCV

FDA-approved treatments for patients with chronic HCV include Epclusa®, an orally administered fixed dose combination of sofosbuvir, an NS5B inhibitor, and velpatasvir, an NS5A inhibitor, Harvoni®, a fixed dose combination sofosbuvir and ledipasvir, an NS5A inhibitor, Vosevi®, a fixed dose triple combination of sofosbuvir, velpatasvir and voxilaprevir, a NS3/4A protease inhibitor, and Sovaldi®, an NS5B inhibitor marketed by Gilead Sciences, Inc., Mavyret®, the combination of glecaprevir, a NS3/4A protease inhibitor, and pibrentasvir, a NS5A inhibitor, marketed by AbbVie Inc., and Zepatier®, the combination of elbasvir, a NS5A inhibitor and grazoprevir, a NS3/4A protease inhibitor, marketed by Merck & Co., Inc., In addition to the branded products, Gilead launched and markets authorized generic copies of Epclusa and Harvoni through its subsidiary, Asegua Therapeutics. LLC. We are not aware of any investigational agents in late-stage development in the US although there may be other investigational agents for HCV in various stages of clinical development in other parts of the world.

Commercialization

We currently believe that we can maximize the value of our product portfolio by retaining global development rights to our product candidates. However, to further maximize the value of product candidates that are authorized or approved for sale, we may seek collaborations that allow us to access and leverage commercialization expertise and resources of collaborators in certain markets. To assist in the commercialization in the US of any product candidates we successfully develop, we may enter into co-promotion arrangements with third parties that have existing commercial infrastructure. Outside the US, we may enter into commercial license agreements. Currently, we do not have any sales, marketing or commercial product distribution infrastructure and we do not have any existing arrangements with third parties to commercialize our product candidates in the US or elsewhere.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our nucleotide therapeutic products for viral diseases, including our purine nucleotide compounds for SARS-CoV-2 and HCV. We seek to protect our proprietary compounds and methods of treatment for viral diseases using our nucleotide compounds, alone and in combination with other therapeutic agents, in addition to dosage forms, dosing regimens and formulations for their administration. We also seek protection on the manufacturing process for the production of our nucleotide compounds. Our success also depends on our ability to operate without infringing, misappropriating or otherwise violating on the proprietary rights of others and to prevent others from infringing, misappropriating or otherwise violating our proprietary rights.

Our policy is to seek to protect our proprietary position by filing US and foreign patent applications covering our proprietary technologies, inventions, and improvements that are important to the development and implementation of our business. In addition, we currently plan to seek patent term adjustments, restorations, and/or patent term extensions where applicable in the US, Europe and other jurisdictions. We also rely on trade secrets, know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our proprietary position. Additionally, we expect to benefit, where appropriate, from statutory frameworks in the US, Europe and other countries that provide a period of regulatory data exclusivity to compensate for the time required for regulatory approval of our drug products.

As of February 1, 2023, we are the sole owner of fifteen patent families covering our product candidates and proprietary nucleotide compounds, which include composition of matter, pharmaceutical compositions, methods of use, and processes of manufacture as described in more detail below. Our owned patent estate as of February 1, 2023, on a worldwide basis, includes more than 250 pending, granted, or allowed patent applications with fourteen issued US patents, eight pending US non-provisional applications, four pending US provisional applications, five pending international patent applications filed under the Patent Cooperation Treaty (“PCT”), and more than 200pending or granted patent applications that have entered the national phase of prosecution in countries outside the US.

As of February 1, 2023, we are the exclusive licensee of three patent families from MSD International GmbH (Merck, Sharp & Dohme Corp.) covering composition of matter, process of preparation, and formulations of the NS5A inhibitor ruzasvir (MK-8408), which collectively include two issued US patents, granted patents in France, Great Britain, and Germany and one pending US patent application and one pending patent application in the EPO.

The exclusivity terms of our patents depend upon the laws of the countries in which they are obtained. In the countries in which we currently file, the patent term is 20 years from the earliest date of filing of a non-provisional patent application. The term of a US patent may be extended to compensate for the time required to obtain regulatory approval to sell a drug (a patent term extension) or by delays encountered during patent prosecution that are caused by the US Patent and Trademark Office (referred to as patent term adjustment). For example, the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act, permits a patent term extension for FDA-approved new chemical entity drugs of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review and diligence during the review process. Patent term extensions in the US cannot extend the term of a patent beyond a total of 14 years from the date of product approval, only one patent covering an approved drug or its method of use may be extended, and only those claims covering the approved drug, or an approved method for using it may be extended. A similar kind of patent extension, referred to as a Supplementary Protection Certificate, is available in the EU. Legal frameworks are also available in certain other jurisdictions to extend the term of a patent. We currently intend to seek patent term extensions on any of our issued patents in any jurisdiction where we have a qualifying patent and the extension is available; however, there is no guarantee that the applicable regulatory authorities, including the FDA in the US, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions. Further, even if our patent is extended, the patent, including the extended portion of the patent, may be held invalid or unenforceable by a court of final jurisdiction in the US or a foreign country.

Current issued patents and patent applications covering the composition of matter for our present clinical candidates AT-511, bemnifosbuvir, AT-281 (the free base of AT-752), and AT-752 will expire on dates ranging from 2036 to 2038, if the applications are issued and held valid by a court of final jurisdiction if challenged, and without regard to any possible patent term adjustments or extensions. Current patent applications covering the use of AT-511 and bemnifosbuvir for the treatment of SARS-CoV-2 will expire on dates ranging from 2040 to 2041, if the applications are issued and held valid by a court of final jurisdiction if challenged, and without regard to any possible patent term adjustments or extensions. Current issued patents and patent applications covering the use of AT-511 and bemnifosbuvir for the treatment of HCV will expire on dates ranging from 2036 to 2042, if the applications are issued and held valid by a court of final jurisdiction if challenged, and without regard to any possible patent term adjustments or extensions. Current patent applications covering the use of AT-281 and AT-752 for the treatment of dengue fever will expire on dates ranging from 2036 to 2043, if the applications are issued and held valid by a court of final jurisdiction if challenged, and without regard to any possible patent term adjustments or extensions.

However, any of our patents, including patents that we may rely on to protect our market for approved products, may be held invalid or unenforceable by a court of final jurisdiction. Alternatively, we may decide that it is in our interest to settle a litigation in a manner that affects the term or enforceability of our patent. Changes in either the patent laws or in interpretations of patent laws in the US and other jurisdictions may diminish our ability to protect our inventions and enforce our intellectual property rights. Accordingly, we cannot predict the breadth or enforceability of claims that have been or may be granted on our patents or on third-party patents. The pharmaceutical and biotechnology industries are characterized by extensive litigation regarding patents and other intellectual property rights. Our ability to obtain and maintain our proprietary position for our nucleotide compounds and the use of these compounds will depend on our success in enforcing patent claims that have been granted or may grant. We do not know whether any of the pending patent applications that we have filed or may file or license from third parties will result in the issuance of any additional patents. The issued patents that we own or may receive in the future may be challenged, invalidated, or circumvented, and the rights granted under any issued patents may not provide us with sufficient protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may be able to independently develop

and commercialize drugs with similar mechanisms of action and/or duplicate our methods of treatments or strategies without infringing our patents. Because of the extensive time required for clinical development and regulatory review of a drug we may develop, it is possible that, before any of our drugs can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of any such patent. For more information regarding risks relating to intellectual property, see Part I, Item 1A. “Risk Factors—Risks Related to Intellectual Property.”

Our patent families, as of February 1, 2023, are further described below.

AT-511 and bemnifosbuvir

We own a first patent family that describes AT-511 or a pharmaceutically acceptable salt thereof (for example, bemnifosbuvir), pharmaceutical compositions of AT-511 or the pharmaceutical salts thereof, and methods to treat HCV using AT-511 or a salt thereof. This family consists of seven issued US patents (US Pat. Nos. 9,828,410; 10,000,523; 10,005,811; 10,239,911; 10,815,266; 10,870,672; 10,870,673) and one pending US applications covering AT-511 or a pharmaceutically acceptable salt thereof, related compounds and their pharmaceutical compositions. This patent family is now also in the national stage of prosecution or granted in the African Regional Intellectual Property Organization (“ARIPO”), Australia, Brazil, Canada, China, Colombia, the Eurasian Patent Office (“EAPO”), Egypt, the European Patent Office (“EPO”), Georgia, Hong Kong, Indonesia, Israel, India, Japan, Korea, Mexico, Macao, Malaysia, Nigeria, New Zealand, the Philippines, Russia, Saudi Arabia, Singapore, Thailand, Vietnam, Ukraine, South Africa, and the United Arab Emirates. We have more than 20 foreign patents granted or allowed, and more than 20 pending patent applications. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2036, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We also own a second patent family that specifically covers bemnifosbuvir, pharmaceutical compositions, and methods to treat HCV using bemnifosbuvir. This family includes two issued US patents (US Pat. No. 10,519,186, and US Patent No. 10,906,938,) and one pending US application covering bemnifosbuvir. This family is currently in the national phase of prosecution in Argentina, ARIPO, Australia, Brazil, Canada, China, Colombia, the EAPO, the EPO, Georgia, Hong Kong, Indonesia, Israel, India, Japan, Korea, Mexico, Malaysia, Nigeria, New Zealand, the Philippines, Russia, Singapore, Taiwan, Thailand, Vietnam, Ukraine, Uzbekistan, and South Africa. We have over ten granted foreign patents and over 25 pending applications. The expected year of expiration for this patent family, if issued, valid and enforceable, is 2038, without regard to any extensions, adjustments, or restorations of term that may be available under US or other national laws.

We own two patent families that disclose methods for the treatment of SARS-CoV-2 using AT-511 or bemnifosbuvir. These families include one granted US patent (US Patent No. 10,874,687), three pending US applications and applications pending in Argentina, ARIPO, Australia, Bahrain, Brazil, Canada, Chile, China, Columbia, Ecuador, Egypt, the EPO, the EAPO, Georgia, India, Israel, Japan, Jordan, Kuwait, Libya, Malaysia, Mexico, Morocco, New Zealand, Nicaragua, Nigeria, Oman, Philippines, Russia, Saudi Arabia, Singapore, South Africa, South Korea, Taiwan, Thailand, Tunisia, Uzbekistan, and Vietnam. The expected year of expiration for patents issued from these families, if valid and enforceable, is 2040 or 2041, without regard to any extensions, adjustments, or restorations of term that may be available under US or other national laws.

We own a fifth patent family that discloses the use of AT-511 or a pharmaceutically acceptable salt thereof for the treatment or prevention of a positive-stranded RNA virus infection, including a *Flaviviridae* viral infection such as dengue, West Nile, or yellow fever. This family consists of one pending application and one issued patent (US Patent No. 10,946,033) and is currently pending or granted in Australia, Brazil, Canada, China, the EAPO, the EPO, Hong Kong, Indonesia, Japan, Korea, Malaysia, Nigeria, Russia, Singapore, Thailand, Vietnam, and South Africa. We have over 30 foreign patents granted and over 20 pending patent applications. The expected year of expiration for this patent family, if issued, valid and enforceable, is 2037, without regard to any extensions, adjustments, or restorations of term that may be available under US or other national laws.

We own a sixth patent family that discloses the use of AT-511 and bemnifosbuvir for the treatment of HCV in patients with cirrhosis of the liver. This family includes one pending US application. This family is currently in the national phase of prosecution in China, the EPO, Hong Kong, Japan, Korea, Russia, and Taiwan. The expected year of expiration for this patent family, if issued, valid and enforceable, is 2039, without regard to any extensions, adjustments, or restorations of term that may be available under US or other national laws.

We own a seventh patent family that describes methods to treat mutant or resistant forms of the SARS-CoV-2 virus. This family consists of one international application filed under the PCT, as well as one application in Argentina and one application in Taiwan. The expected year of expiration for patents issued from non-provisional patent applications filed on the basis of this patent application, if valid and enforceable, is 2041, without regard to adjustments of term that may be available under US or other national laws.

We also own an eighth patent family that discloses methods for manufacturing AT-511 and bemnifosbuvir. This family consists of one pending US application. The expected year of expiration for patents issued from non-provisional patent applications filed on the basis of these provisional patent applications, if valid and enforceable, is 2041, without regard to adjustments of term that may be available under US or other national laws.

We also own a ninth patent family that discloses additional processes for the manufacture of AT-511 and bemnifosbuvir. This family consists of one international application field under the PCT. The expected year of expiration for patents issuing from these non-provisional patent applications, if valid and enforceable, is 2041, without regard to any adjustments of term that may be available under US or other national law.

We also own a tenth patent family that discloses new morphic forms of bemnifosbuvir. This family consists of one international application filed under the PCT, as well as one pending application in Canada. The expected year of expiration for patents issued from non-provisional patent applications filed on the basis of this patent application, if valid and enforceable, is 2042, without regard to adjustments of term that may be available under US or other national laws.

AT-281 and AT-752

The first patent family described above also describes AT-281, a pharmaceutically acceptable salt thereof (for example, AT-752) and pharmaceutical compositions of AT-281 or a pharmaceutical salt thereof and their use to treat HCV infection, including issued US Patent No. 10,875,885.

The second patent family described above also describes AT-752 and pharmaceutical compositions of AT-752, including in US Patent No. 10,906,928. One of these pending US applications in this patent family covers AT-752 and pharmaceutical compositions of AT-752.

The fifth patent family described above also includes a disclosure of the use of AT-281 or a pharmaceutically acceptable salt thereof for the treatment or prevention of an RNA viral infection, including dengue fever (US Patent No. 10,946,033), yellow fever, and Zika virus. Therefore, we have three patent families that describe AT-281 or AT-752 and methods of treatment for viral infections using AT-281 or AT-752.

We own another patent family that consists of three provisional US applications that disclose advantageous dosage forms of AT-752, dosage regimens of AT-752, and combination therapies comprising AT-752 for the treatment of dengue fever. The expected year of expiration for patents issuing from these non-provisional patent applications, if valid and enforceable, is 2043, without regard to any adjustments of term that may be available under US or other national law.

Ruzasvir

We have exclusively licensed three patent families from MSD International GmbH (Merck, Sharp & Dohme Corp.) covering composition of matter, process of preparation, and formulations of ruzasvir (MK-8408), a pan-genotype NS5A inhibitor to treat HCV. The family covering the composition of matter includes one granted US patent (US Patent No. 9,555,038), and granted patents in France, Great Britain, and Germany. The expected expiration date is in 2034. The family describing a process of preparation

includes one granted US patent (US Patent No. 10,457,690), with an expected expiration date in 2036 The family describing formulations includes one pending US patent application and one pending patent application in the EPO, which if granted, is expected to expire in 2039.

We also solely own an international application filed under the PCT covering the combination of bemnifosbuvir and ruzasvir, which if granted, will have an expiration date in 2042.

Government Regulation and Product Approval

Government authorities in the US, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and export and import of products such as those we are developing. A new drug must be approved by the FDA through the new drug application ("NDA"), process before it may be legally marketed in the US.

US Drug Development Process

In the US, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act ("FDCA") and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

The process required by the FDA before a drug may be marketed in the US generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in accordance with FDA's good laboratory practice requirements and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board ("IRB"), or ethics committee at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practice requirements ("GCPs") to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA after completion of all pivotal trials;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current good manufacturing practice ("cGMP"), requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity, and of selected clinical investigation sites to assess compliance with GCPs; and
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the US.

Prior to beginning the first clinical trial with a product candidate in the US, a sponsor must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an IND product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the investigational product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. Once submitted, the IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30- day time period, raises safety concerns or questions about the proposed clinical

trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. While the IND is active, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or *in vitro* testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

Furthermore, an independent IRB or ethics committee for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site and must monitor the study until completed. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the investigational product has been associated with unexpected serious harm to patients.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

Phase 1: The product candidate is initially introduced into healthy human subjects, and in some cases, patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.

Phase 2: The product candidate is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

Phase 3: The product candidate is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

Post-approval trials, sometimes referred to as Phase 4 studies, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the meeting at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug 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 drug. In addition, 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.

US Review and Approval Process

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical and other non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once filed, the FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. Under the Prescription Drug User Fee Act ("PDUFA"), guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision after it the application is submitted.

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

Before approving an NDA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP and adequate to assure consistent production of the product within required specifications. Additionally, before approving a NDA, the FDA may inspect one or more clinical sites to assure compliance with GCPs.

After the FDA evaluates an NDA, it will issue an approval letter or a Complete Response Letter ("CRL"). An approval letter authorizes commercial marketing of the drug with prescribing information for specific indications. 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 usually describes the specific deficiencies in the NDA identified by the FDA and may require additional clinical data, such as an additional clinical trials or other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a CRL is issued, the sponsor must resubmit the NDA addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA does not satisfy the criteria for approval.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations or restrictions on the indicated uses for which such product may be marketed. For example, the FDA may approve the NDA with a Risk Evaluation and Mitigation Strategy (“REMS”), to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may also require one or more Phase 4 post-approval studies and surveillance to further assess and monitor the product’s safety and effectiveness after commercialization and may limit further marketing of the product based on the results of these post-approval studies. In addition, new government requirements, including those resulting from new legislation, may be established, or the FDA’s policies may change, which could impact the timeline for regulatory approval or otherwise impact ongoing development programs.

In addition, the Pediatric Research Equity Act (“PREA”), requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Emergency Use Authorization

The Commissioner of the FDA, under delegated authority from the Secretary of Health and Human Services (“HHS”) may, under certain circumstances in connection with a declared public health emergency, allow for the marketing of a product that does not otherwise comply with FDA regulations by issuing an EUA for such product. Before an EUA may be issued by HHS, the Secretary must declare an emergency based a determination that public health emergency exists that effects or has the significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents (“CBRN”), or a specified disease or condition that may be attributable to such CBRN. On February 4, 2020, the HHS Secretary determined that there is such a public health emergency that involves SARS-CoV-2, the virus that causes the COVID-19 infection. Once the determination of the threat or emergency has been made, the Secretary of HHS must then declare that an emergency exists justifying the issuance of EUAs for certain types of products (referred to as EUA declarations). On March 27, 2020, the Secretary of HHS declared - on the basis of his determination of a public health emergency that has the potential to affect national security or the health and security of US citizens living abroad that involves SARS-CoV-2 - that circumstances exist justifying authorization of drugs and biologics during the COVID-19 pandemic, subject to the terms of any EUA that is issued.

Once an EUA declaration has been issued, the FDA can issue EUAs for products that fall within the scope of that declaration. To issue an EUA, the FDA Commissioner must conclude that (1) the CBRN that is referred to in the EUA declaration can cause serious or life-threatening diseases or conditions; (2) based on the totality of scientific evidence available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing the disease or condition attributable to the CBRN and that the product's known and potential benefits outweigh its known and potential risks; and (3) there is no adequate, approved, and available alternative to the product. Products subject to an EUA must still comply with the conditions of the EUA, including labeling and marketing requirements. Moreover, the authorization to market products under an EUA is limited to the period of time the EUA declaration is in effect, and the FDA can revoke an EUA in certain circumstances.

Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates. For example, the FDA Fast Track program is intended to expedite or facilitate the process for reviewing product candidates that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. With regard to a Fast Track product candidate, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for Breakthrough Therapy designation to expedite its development and review. A product candidate can receive Breakthrough Therapy designation if preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, 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 designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

Any marketing application for a drug submitted to the FDA for approval, including a product with a Fast Track designation or Breakthrough Therapy designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. An NDA is eligible for priority review if the product candidate is designed to treat a serious condition, and if approved, would provide a significant improvement in safety or effectiveness compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an NDA designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six months of the filing date as compared to ten months for review of new molecular entity NDAs under its current PDUFA review goals.

In addition, a product candidate may be eligible for accelerated approval. Product candidates intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA generally requires that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled confirmatory clinical trials to verify and describe the predicted clinical benefit. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required clinical trials in a timely manner, or if such trials fail to verify the predicted clinical benefit. In addition, the FDA currently requires pre-approval of promotional materials as a condition for accelerated approval, which could adversely impact the timing of the commercial launch of the product.

Fast Track designation, Breakthrough Therapy designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process. Even if a

product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Post-approval Requirements

Any products manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of 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 program fees for any marketed products.

Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements upon drug manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon NDA holders and any third-party manufacturers that NDA holders may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

The FDA may withdraw 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 studies to assess new safety risks, or imposition of distribution restrictions 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 untitled letters;
- clinical holds on clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of drug products. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's

labeling and that differ from those tested and approved by the FDA. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict marketers' communications on the subject of off-label use of their products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined companies from engaging in off-label promotion. The FDA and other regulatory agencies have also required that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labelling.

Marketing Exclusivity

Marketing exclusivity provisions authorized under the FDCA can delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent data exclusivity within the US to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application ("ANDA"), or an NDA submitted under Section 505(b)(2) ("505(b)(2) NDA"), submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

The FDCA alternatively provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to any preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of marketing exclusivity available in the US. Pediatric exclusivity provides for an additional six months of marketing exclusivity attached to another period of exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA. The issuance of a written request does not require the sponsor to undertake the described clinical trials.

Other Healthcare Laws

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws include, without limitation, US federal and state anti-kickback, fraud and abuse, false claims, pricing reporting, and physician payment transparency laws and regulations regarding drug pricing and payments or other transfers of value made to physicians and other licensed healthcare professionals as well as similar foreign laws in the jurisdictions outside the US. Such foreign laws and regulations may be broader in scope than the provisions described above and may apply regardless of payor. These laws and regulations may differ from one another in significant ways, thus further complicating compliance efforts. For instance, in the EU, many EU member states have adopted specific anti-gift statutes that further limit commercial practices for medicinal products, in particular vis-à-vis healthcare professionals and organizations. Additionally, there has been a recent trend of increased regulation of payments and transfers of value provided to healthcare professionals or entities and many EU member states have adopted national "Sunshine Acts" which impose reporting and transparency requirements (often on an annual basis), similar to the requirements in the US, on pharmaceutical companies. Certain countries also mandate implementation of commercial compliance programs, or require disclosure of marketing expenditures and pricing information. Violation of any of such laws or any other governmental regulations

that apply may result in significant penalties, including, without limitation, administrative civil and criminal penalties, damages, disgorgement fines, additional reporting requirements and oversight obligations, contractual damages, the curtailment or restructuring of operations, exclusion from participation in governmental healthcare programs and/ or imprisonment.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidate for which we may seek regulatory approval. Sales in the US and in foreign jurisdictions will depend, in part, on the availability of sufficient coverage and adequate reimbursement from third-party payors, which include government health programs such as Medicare, Medicaid, TRICARE and the Veterans Administration, as well as managed care organizations and private health insurers. Prices at which we or our customers seek reimbursement for our product candidates can be subject to challenge, reduction or denial by third-party payors.

The process for determining whether a third-party payor will provide coverage for a product is typically separate from the process for setting the reimbursement rate that the payor will pay for the product. In the US, there is no uniform policy among payors for coverage or reimbursement. Decisions regarding whether to cover any of a product, the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies, but also have their own methods and approval processes. Therefore, 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 can require manufacturers to provide scientific and clinical support for the use of a product to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product that receives approval. Third-party payors may not consider our product candidates to be medically necessary or cost-effective compared to other available therapies, or the rebate percentages required to secure favorable coverage may not yield an adequate margin over cost or may not enable us to maintain price levels sufficient to realize an appropriate return on our investment in drug development. Additionally, decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product.

Healthcare Reform

In the US and in foreign jurisdictions, there has been, and continues to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect the profitable sale of product candidates.

Among policy makers and payors in the US, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the US, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the “ACA”) was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly affected the pharmaceutical industry. The ACA increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1%; required collection of rebates for drugs paid by Medicaid managed care organizations; required manufacturers to participate in a coverage gap discount program, in which manufacturers must agree to offer point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D; imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell certain “branded prescription drugs” to specified federal government programs, implemented a

new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected; expanded eligibility criteria for Medicaid programs; created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare and Medicaid Innovation at the Centers for Medicare & Medicaid Services ("CMS") to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial and political challenges to certain aspects of the ACA. On June 17, 2021, the US Supreme Court dismissed the most recent judicial challenge to the ACA without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to health care, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. In addition, on January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. In addition, on March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, beginning January 1, 2024.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was enacted into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), 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 HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated.

Individual states in the US have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, certain individual states as well as regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine which drugs and suppliers will be included in their healthcare programs. The states of Louisiana and Washington used bidding procedures in 2019 and more recently Minnesota did so in 2021 to secure contracts with suppliers of HCV antiviral therapeutics for certain populations including those covered by Medicare and those in correctional institutions. Other states are currently engaged in similar discussions. Furthermore, there has been increased interest by third party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

In the EU, on December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment ("HTA") was adopted. While the Regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim.

Once the Regulation becomes applicable, it will have a phased implementation depending on the concerned products. This regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of m emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

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

Data Privacy & Security

Numerous state and federal laws, regulations and standards govern the collection, use, access to, confidentiality and security of health-related and other personal information, and could apply now or in the future to our operations or the operations of our partners. In the US, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal information. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Further, certain foreign laws govern the privacy and security of personal data, including health-related data. For example, the EU General Data Protection Regulation ("GDPR") imposes strict requirements for processing the personal data of individuals within the European Economic Area. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. Further, from January 1, 2021, companies have had to comply with the GDPR and also the UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR, i.e., fines up to the greater of €20 million (£17.5 million) or 4% of global turnover.

Government Regulation Outside of the US

In addition to regulations in the US, we are subject to a variety of regulations in other jurisdictions, such as EU, governing, among other things, clinical trials, marketing authorization and any commercial sales and distribution of our products once approved. Whether or not we obtain FDA approval for a product candidate, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. The requirements and process governing the conduct of clinical trials, approval process, product licensing, pricing and reimbursement vary from country to country. Failure to comply with applicable foreign regulatory requirements, may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Non-clinical studies and clinical trials

Similarly to the US, the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls.

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 good laboratory practice (“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-labelling 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 trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Conference on Harmonization ("ICH") guidelines on Good Clinical Practices ("GCP") as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU member states, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation ("CTR") which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database.

While the Clinical Trials Directive required a separate clinical trial application ("CTA") to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application for multi-center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation.

The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

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 (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the EU Clinical Trials Directive 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.

Medicines used in clinical trials must be manufactured in accordance with Good Manufacturing Practice ("GMP"). Other national and EU-wide regulatory requirements may also apply.

Marketing Authorization

In order to market our future product candidates in the EU and many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EU, medicinal product candidates can only be commercialized after obtaining a marketing authorization ("MA"). To obtain regulatory approval of a product candidate under EU regulatory systems, we must submit a MA application ("MAA"). The process for doing this depends, among other things, on the nature of the medicinal product. There are two types of MAs:

- "Centralized MA" are issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Product for Human Use ("CHMP") of the European Medicines Agency ("EMA") and are valid throughout the EU. The centralized procedure is mandatory for certain types of product candidates, such as: (i) medicinal products

derived from biotechnology processes, such as genetic engineering, (ii) designated orphan medicines, (iii) medicinal products containing a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, neurodegenerative diseases, diabetes, auto-immune and other immune dysfunctions and viral diseases and (iv) advanced therapy medicinal products ("ATMPs") such as gene therapy, somatic cell therapy or tissue-engineered medicines. The centralized procedure is optional for product candidates containing a new active substance not yet authorized in the EU, or for product candidates that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

- "National MAs" are issued by the competent authorities of the EU member states, only cover their respective territory, and are available for product candidates not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU member state, this national MA can be recognized in another member state through the mutual recognition procedure. If the product has not received a national MA in any member state at the time of application, it can be approved simultaneously in various member states through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the reference member state.

Under the centralized procedure the maximum timeframe for the evaluation of a MAA by the EMA is 210 days.

In the EU, innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the Priority Medicines ("PRIME") scheme, which provides incentives similar to the breakthrough therapy designation in the US In March 2016, the EMA launched an initiative, the PRIME scheme, a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product developers that benefit from PRIME designation can expect to be eligible for accelerated assessment but this is not guaranteed. 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 MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Moreover, in the EU, a "conditional" MA may be granted in cases where all the required safety and efficacy data are not yet available. The conditional MA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and has to be renewed annually until fulfillment of all the conditions. Once the pending studies are provided, it can become a "standard" MA. However, if the conditions are not fulfilled within the timeframe set by the EMA, the MA ceases to be renewed. Furthermore, MA 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 MA is close to the conditional MA 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 a MA. However, unlike the conditional MA, the applicant does not have to provide the missing data and will never have to. Although the MA "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the MA is withdrawn in case the risk-benefit ratio is no longer favorable.

Under the above described procedures, in order to grant the MA, the EMA or the competent authorities of the EU 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. MAs have an initial duration of five years. After these five years, the authorization may be renewed for an unlimited period on the basis of a reevaluation of the risk-benefit balance.

Data and Marketing Exclusivity

The EU also provides opportunities for data and market exclusivity. Upon receiving MA, reference products generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, the data exclusivity period prevents generic or biosimilar applicants from relying on the pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial MA of the reference product in the EU. The overall 10-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those 10 years, the MA 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. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity.

Pediatric Development

In the EU, MAAs for new medicinal products have to include the results of studies conducted in the pediatric population, in compliance with a pediatric investigational plan ("PIP") agreed with the EMA's Pediatric Committee ("PDCO"). The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data is not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all the EU member states and study results are included in the product information, even when negative, the product is eligible for six months' supplementary protection certificate extension (if any is in effect at the time of approval) or, in the case of orphan pharmaceutical products, a two year extension of the orphan market exclusivity is granted.

The aforementioned EU rules are generally applicable in the European Economic Area ("EEA") which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland.

Failure to comply with EU and member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

Brexit and the Regulatory Framework in the United Kingdom

Since the end of the Brexit transition period on January 1,2021, Great Britain (England, Scotland and Wales) has not been directly subject to EU laws, however under the terms of the Ireland/Northern Ireland Protocol, EU laws generally apply to Northern Ireland. The EU laws that have been transposed into United Kingdom ("UK") law through secondary legislation remain applicable in Great Britain. However, under the Retained EU Law (Revocation and Reform) Bill 2022, which is currently before the UK parliament, any retained EU law not expressly preserved and "assimilated" into domestic law or extended by ministerial regulations (to no later than 23 June 2026) will automatically expire and be revoked by

December 31, 2023. However, new legislation such as the (EU) CTR is not applicable in Great Britain ("GB"). Under the Medicines and Medical Devices Act 2021, the Secretary of State or an 'appropriate authority' has delegated powers to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices.

Since January 1, 2021, the Medicines and Healthcare products Regulatory Agency ("MHRA") has been the UK's standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales, and Scotland, together, GB; broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA.

The UK regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into UK law, through secondary legislation). On January 17, 2022, the MHRA launched an eight-week consultation on reframing the UK legislation for clinical trials. The consultation closed on March 14, 2022 and aims to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The outcome of the consultation is being closely watched and will determine whether the UK chooses to align with the (EU) CTR or diverge from it to maintain regulatory flexibility.

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, including a 150-day assessment and a rolling review procedure. All existing EU MAs for centrally authorized products were automatically converted or grandfathered into UK MAs, effective in GB (only), free of charge on January 1, 2021, unless the MA holder opted-out. In order to use the centralized procedure to obtain a MA that will be valid throughout the EEA, companies must be established in the EEA. Therefore since Brexit, companies established in the UK can no longer use the EU centralized procedure and instead an EEA entity must hold any centralized MAs. In order to obtain a UK MA to commercialize products in the UK, an applicant must be established in the UK and must follow one of the UK national authorization procedures or one of the remaining post-Brexit international cooperation procedures to obtain an MA to commercialize products in the UK.

There will be no pre-MA orphan designation. Instead, the MHRA will review applications for orphan designation in parallel to the corresponding MA application. The criteria are essentially the same, but have been tailored for the market, i.e., the prevalence of the condition in GB, rather than the EU, must not be more than five in 10,000. Should an orphan designation be granted, the period of market exclusivity will be set from the date of first approval of the product in GB.

Human Capital Resources

As of February 20, 2023, we had 70 full-time employees, including 23 employees with M.D., Ph.D. or Pharm.D. degrees. Of these full-time employees, 49 employees are engaged in research and development activities. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Our human capital resource priorities include attracting, recruiting, retaining, incentivizing and integrating our existing and new employees. The principal purpose of our competitive equity and cash compensation and benefits programs is to promote and support these priorities. We consider our human capital resources strategy to be comprehensive and built to foster our core way of working which is grounded on the principles of scientific rigor in a collaborative, entrepreneurial, and results-oriented manner. We plan to continue to evaluate our suite of human capital resources as we grow.

Organization

Atea Pharmaceuticals, Inc. was incorporated in July 2012 and began principal operations in March 2014. The Company is located in Boston, Massachusetts. Atea Pharmaceuticals Securities Corporation, a Massachusetts corporation incorporated in 2016, is a wholly owned subsidiary of Atea Pharmaceuticals, Inc.

Available Information

We file or furnish electronically with the Securities and Exchange Commission ("SEC") our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, proxy statements and other information, as well as amendments to those reports. These and other SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov. We make available on our website at https://ateapharma.com, under "Investors," free of charge, copies of these reports as soon as reasonably practicable after filing or furnishing these reports with the SEC.

Information about our Executive Officers and Directors

The following table sets forth the name, age and position of each of our executive officers and directors as of the date of this Annual Report on Form 10-K.

Name	Age	Position
Executive Officers		
Jean-Pierre Sommadossi, Ph.D.	66	President and Chief Executive Officer and Chairman of the Board of Directors
Andrea Corcoran	60	Chief Financial Officer, Executive Vice President, Legal and Secretary
Janet Hammond, M.D., Ph.D.	62	Chief Development Officer
Maria Arantxa Horga, M.D.	54	Chief Medical Officer
John Vavricka	59	Chief Commercial Officer
Wayne Foster	54	Executive Vice President and Chief Accounting Officer
Directors		
Franklin Berger (1)(2)	73	Director (Lead Director)
Jerome Adams, M.D. (3)(4)	48	Director
Barbara Duncan (1)(3)	58	Director
Bruno Lucidi (1)(2)	63	Director
Polly A. Murphy, D.V.M., Ph.D. (3)(4)	58	Director
Bruce Polsky, M.D. (2)(4)	68	Director

(1) Member of the Audit Committee.
(2) Member of the Compensation Committee.
(3) Member of the Nominating and Corporate Governance Committee.
(4) Member of the Strategy and Public Policy Committee.

Executive Officers

Jean-Pierre Sommadossi, Ph.D., is the founder of our company and has served as our President and Chief Executive Officer and as Chairman of our Board since July 2012. Prior to that, he co-founded and held several roles at Idenix Pharmaceuticals, Inc., a biopharmaceutical company, from 1998 to 2010, including Principal Founder and Chief Executive Officer and Chairman. Dr. Sommadossi also co-founded Pharmasset, Inc., a biopharmaceutical company, in 1998. Dr. Sommadossi has also served on the board of directors of ABG Acquisition Corporation since February 2021, as Chairman of the board of directors of Panchrest, Inc., a marketing authorized representative in healthcare, since 2013, and Chairman of the board of directors of Biothea Pharma, Inc., a biotechnology company since 2021. Dr. Sommadossi has also served as a member of the board of directors of The BioExec Institute since 2004. Previously, Dr. Sommadossi served as Chairman of the board of directors of Kezar Life Sciences, Inc., a biopharmaceutical company, from June 2015 to May 2022, Vice Chairman of the board of directors of Rafael Pharmaceuticals, Inc., a biopharmaceutical company, from October 2016 to November 2020 and as Chair of the board of directors of PegaOne, Inc., a biopharmaceutical company from September 2020 to January 2021. Dr. Sommadossi also served as a member of the Harvard Medical School Discovery Council from 2010 to 2021 Dr. Sommadossi received his Ph.D. and Pharm.D. degrees from the University of Marseilles in France. We believe that Dr. Sommadossi's extensive scientific, operational, strategic and management experience in the biotech industry qualifies him to serve on our Board.

Andrea Corcoran has served as our Chief Financial Officer since October 2020, our Secretary since September 2014 and our Executive Vice President, Legal since December 2013. Ms. Corcoran also

served as Executive Vice President, Administration from September 2014 to October 2020. Prior to joining us, Ms. Corcoran served as Senior Vice President, Strategy and Finance at iBio, Inc., a biotechnology company, from 2011 to 2012, as General Counsel and Secretary at Tolerx, Inc., a biopharmaceutical company, from 2007 to 2011, and as Executive Vice President of Idenix Pharmaceuticals, Inc. from 1998 to 2007. Ms. Corcoran received her J.D. from Boston College Law School and her B.S. from Providence College.

Janet Hammond, M.D., Ph.D., has served as our Chief Development Officer since August 2020. Prior to joining us, Dr. Hammond served at AbbVie, Inc., a biopharmaceutical company, from November 2016 to August 2020 as Vice President and Therapeutic Area Head for General Medicine and Infectious Disease Development and at F. Hoffmann-La Roche from March 2011 to November 2016 as Senior Vice President, Global Head of Infectious Diseases and Head of Pharmaceutical Research and Early Development China. Dr. Hammond received her M.D. and Ph.D. from the University of Cape Town, South Africa, and her Sc.M. in Clinical Investigation from Johns Hopkins University School of Hygiene and Public Health.

Maria Arantxa Horga, M.D., has served as our Chief Medical Officer since January 2021 and previously served as our Acting Chief Medical Officer since October 2020 and as Executive Vice President, Clinical Sciences since August 2020. Prior to joining us, Dr. Horga served as Vice President, Pharmacovigilance and Medical Affairs at Biohaven Pharmaceuticals from October 2019 to August 2020. Prior to that, Dr. Horga served as Vice President, Global Head of Clinical Program Execution, Site Head of the Roche NY Innovation Center from July 2017 to August 2019, and as Global Head of Translational Medicine, Infectious Diseases at F. Hoffmann-La Roche from 2012 to 2016. Dr. Horga received her M.D. from the Santander School of Medicine and completed her residency in Pediatrics and a fellowship in Pediatric Infectious Diseases at the Mount Sinai School of Medicine.

John Vavricka has served as our Chief Commercial Officer since October 2018. Prior to joining us, Mr. Vavricka cofounded and served as the Chief Executive Officer of Biothea Pharma, Inc., a biotechnology company, from March 2018 to June 2021. Prior to that Mr. Vavricka founded and served as the Chief Executive Officer and President of Iroko Pharmaceuticals, Inc., a global pharmaceuticals company, from 2007 to 2015. Mr. Vavricka received his B.S. from Northwestern University.

Wayne Foster has served as our Executive Vice President, Finance and Chief Accounting Officer since January 2022 and previously served as Senior Vice President, Finance and Administration from December 2019 to January 2022. Prior to joining us, Mr. Foster served as Vice President of Finance at Mersana Therapeutics, Inc., a biopharmaceutical company, from January 2012 to September 2019. Mr. Foster received his B.B.A. from the University of Massachusetts Amherst.

Directors

Franklin Berger has served as a member and the Lead Director of our Board since September 2019. Mr. Berger has served as Founder and Managing Director at FMB Research LLC, a consulting firm, since June 2005. Mr. Berger also has served on the boards of directors of BELLUS Health, Inc. since May 2010, ESSA Pharma Inc. since March 2015, Kezar Life Sciences, Inc. since January 2016, Atreca Inc. since October 2014, Rain Therapeutics Inc. since May 2020 and as lead director of Rain Therapeutics Inc. since April 2021. Mr. Berger previously served on the boards of directors of Tocagen, Inc. from October 2014 to December 2020, of Proteostasis Therapeutics, Inc. from February 2016 to December 2020, and of Five Prime Therapeutics, Inc. from October 2014 to April 2021. Mr. Berger received his B.A. and M.A. from Johns Hopkins University and his M.B.A. from Harvard Business School. We believe that Mr. Berger's financial background and experience as an equity analyst in the biotechnology industry combined with his experience serving on the boards of directors of multiple public companies qualifies him to serve on our Board.

Jerome Adams, M.D., has served as a member of our Board since May 2021. Dr. Adams also has served as Director of Health Equity Initiatives at Purdue University since October 2021. Dr. Adams served as the 20th Surgeon General of the US from September 2017 to January 2021, where he focused on the opioid epidemic and was a member of the COVID-19 Task Force. Prior to that, Dr. Adams served as the State Health Commissioner for the State of Indiana from November 2014 to September 2017, where he presided over Indiana's efforts to deal with state-wide, unprecedented HIV outbreak. Before beginning his

public service in 2014, Dr. Adams was a practicing anesthesiologist and Associate Professor in the Department of Anesthesiology at Indiana University from January 2008 to until September 2017. Earlier in his career, Dr. Adams was a Clinical Research Assistant at Eli Lilly and Company. He has served in leadership positions at a number of professional organizations, including the American Medical Association, the Indiana State Medical Association, and the Indiana Society of Anesthesiologists. Dr. Adams received his B.S. in Biochemistry and B.A. in Psychology from the University of Maryland, Baltimore County, his M.D. from the Indiana University School of Medicine and his M.P.H. from the University of California, Berkeley. We believe that Dr. Adams' extensive public sector experience, including his work on the COVID-19 Task Force, qualifies him to serve on our board.

Barbara Duncan has served as a member of our Board since October 2020. Ms. Duncan served at Intercept Pharmaceuticals, Inc. as Chief Financial Officer and Treasurer from May 2009 to June 2016. Ms. Duncan also has served as Chair of the board of directors of Fusion Pharmaceuticals Inc. since November 2020, on the board of directors of Jounce Therapeutics, Inc. since June 2016, Adaptimmune Therapeutics plc since June 2016, Ovid Therapeutics, Inc. since June 2017, and Halozyme, Inc. since February 2023. Previously, Ms. Duncan served on the boards of directors of Immunomedics, Inc. from March 2019 to October 2020, Innoviva, Inc., from November 2016 through April 2018, Aevi Genomic Medicine, Inc., from June 2015 through January 2020, and ObsEva S.A. from November 2016 to May 2021. Ms. Duncan received her B.A. from Louisiana State University and her M.B.A. from the Wharton School, University of Pennsylvania. We believe Ms. Duncan is qualified to serve on our Board due to her experience in the biotechnology industry and with public companies.

Bruno Lucidi has served as a member of our Board since September 2014. Mr. Lucidi has served as an independent consultant to biotechnology companies since July 2013. Mr. Lucidi served as a Life Sciences Expert at Wallonia Trade and Foreign Investment Agency, an economic development agency, from January 2017 to June 2020. From October 2017 to September 2019, Mr. Lucidi was Chief Executive Officer at AgenTus Therapeutics, a pre-clinical stage biopharmaceutical company. Mr. Lucidi has more than 35 years of experience in the pharmaceutical industry. He held Senior Executive positions at Bristol-Myers Squibb, Johnson and Johnson and GSK and he has been CEO and Chairman of the board of several biopharmaceutical companies in Europe and the US. Mr. Lucidi was trained in Oncology at the Gustave Roussy Institute, Villejuif, France, in Marketing and Strategic Management of Companies at the Ecole Superieure de Commerce, Paris, France, and in Finance, Merger and Acquisitions at the Investment Banking Institute in New York. We believe Mr. Lucidi is qualified to serve on our Board due to his extensive experience in the life sciences industry.

Polly A. Murphy, D.V.M., Ph.D. has served as a member of our Board since August 2020. Dr. Murphy has served as Chief Business Officer at UroGen Pharma, Inc. since August 2020. Prior to that, Dr. Murphy served in various leadership roles at Pfizer, Inc. from September 2008 to August 2020, including as Vice President and Head of Commercial Development Pfizer Oncology Business Unit from January 2019 to August 2020, Vice President and Head of Global Marketing and Commercial Development Pfizer Oncology Business Unit from June 2017 to December 2018, and as Vice President and Head of Strategy and Business Development for Pfizer China from November 2013 to May 2018. Dr. Murphy has served on the board of directors of Celcuity Inc. since September 2022. Dr. Murphy received her D.V.M. and Ph.D. from Iowa State University. We believe Dr. Murphy is qualified to serve on our Board due to her experience in the pharmaceutical industry in business development and commercialization.

Bruce Polsky, M.D., has served as a member of our Board since November 2014. Dr. Polsky is the chair of the Department of Medicine at NYU Langone Hospital – Long Island in Mineola, New York, where he has practiced since May 2015. He also has served as professor and Chair of the Department of Medicine at NYU Long Island School of Medicine and as an Associate Dean at NYU Long Island School of Medicine since February 2019. Dr. Polsky is a leading clinical virologist who played an active role in clinical investigations of HIV/AIDS, HBV, HCV and other viral infections. From December 1998 to May 2015, Dr. Polsky was at Mount Sinai St. Luke's and Mount Sinai Roosevelt Hospitals, where he served as Chair of the Department of Medicine and as Chief of the Division of Infectious Diseases, among other positions. Dr. Polsky received his M.D. from Wayne State University. We believe Dr. Polsky is qualified to serve on our Board due to his extensive clinical experience in the life sciences industry.

Item 1A. Risk Factors.

You should carefully consider the risks and uncertainties described below, as well as the other information in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes and "Management's Discussion and Analysis of Results of Operations and Financial Condition." Our business, financial condition, results of operations or prospects could be materially and adversely affected if any of these risks occurs, and as a result, the market price of our common stock could decline and you could lose all or part of your investment. Our actual results could differ materially and adversely from those anticipated in these forward-looking statements as a result of certain factors, including those set forth below.

Risks Related to COVID-19

There is significant uncertainty around our development of bemnifosbuvir as a potential treatment for COVID-19.

Our development of bemnifosbuvir for the treatment of COVID-19 is in its early stages, and we may not be successful in our development of bemnifosbuvir as a potential treatment for COVID-19. In October 2020, we entered into a license agreement (as amended, "Roche License Agreement") with F. Hoffmann-LaRoche Ltd. and Genentech, Inc. (together, "Roche") under which we granted to Roche an exclusive license to development and commercialization rights related to certain of our compounds, including bemnifosbuvir, outside of the US (other than for certain HCV uses). Together with Roche, in April 2021, we initiated a randomized, double blind, multi-center, placebo-controlled Phase 3 MORNINGSKY clinical trial to study bemnifosbuvir in adult and adolescent patients with mild or moderate COVID-19 in the outpatient setting and we subsequently initiated MEADOWSPRING, a Phase 3 six month follow-up study, to assess the impact of bemnifosbuvir treatment on long-term sequelae of COVID-19 in the patients previously enrolled in MORNINGSKY. Phase 3 clinical trials were begun while two Phase 2 clinical trials evaluating bemnifosbuvir in patients with COVID-19 were ongoing. One of these Phase 2 clinical trials enrolled hospitalized patients and the other Phase 2 MOONSONG clinical trial enrolled outpatients. In October 2021, we, together with Roche, completed MOONSONG, and we announced that we did not meet the primary endpoint of reduction from baseline in the amount of SARS-CoV-2 virus in patients with mild or moderate COVID-19 compared to placebo in the overall study population, of which approximately two-thirds of enrolled patients were low-risk with mild symptoms. In November 2021, Roche notified us that it was terminating the Roche License Agreement effective February 10, 2022. In December 2021, due to the changing COVID-19 treatment landscape, including the availability of new oral antiviral treatment regimens, we determined to discontinue each of the Phase 3 MORNINGSKY and MEADOWSPRING clinical trials. We did not enroll a sufficient number of patients in either Phase 3 study to conduct prespecified statistical analyses. In January 2022 we determined to close out the Phase 2 clinical trial in hospitalized patients.

Nonetheless, we are advancing the development of bemnifosbuvir for the treatment of COVID-19 in high risk non-hospitalized patients pursuing both a mono- and combination strategy. We do not know if either monotherapy or combination therapy approach will be successful. In November 2022, we initiated SUNRISE-3, a global, multicenter, randomized, double blind, placebo-controlled Phase 3 clinical trial evaluating bemnifosbuvir (550 mg BID for 5 days) in at least 1500 high-risk non-hospitalized patients with mild or moderate COVID-19.

In parallel with the conduct of SUNRISE-3, we are also engaging in efforts to discover a proprietary protease inhibitor that could potentially be combined with bemnifosbuvir for the treatment of COVID-19. Our efforts to internally discover and develop a potential protease inhibitor to evaluate in combination with bemnifosbuvir are at a very early stage and we do not know if such efforts will be successful, or if successful, when a protease inhibitor product candidate generated from our discovery efforts may be permitted to enter clinical development. Before we can begin clinical development of a newly discovered protease inhibitor product candidate, or any other product candidate, we will need to complete extensive preclinical studies to support the submission of an IND to the FDA or CTA to a comparable regulatory authority outside the US.

Conducting preclinical testing of any product candidate and the related manufacture of sufficient quantities of material that can be used in clinical trials, is a complex, lengthy, time consuming and

expensive process. As a result, we cannot be certain that we will be able to submit such INDs or CTAs on the timelines we expect, if at all, and we cannot be certain that regulatory authorities will allow clinical trials of a protease inhibitor that we newly discover to begin.

Alternatively, we may in-license or acquire the rights to develop and commercialize a protease inhibitor drug candidate from a third-party. Proposing, negotiating and implementing acquisition or in-license of a protease inhibitor or any other product candidate that may be combined with bemnifosbuvir for the potential treatment of COVID-19 may be a lengthy and complex process. Other companies, including those with substantially greater financial, marketing and sales resources, may compete with us for the acquisition of such product candidates. We may not be able to acquire the rights to additional product candidates on terms that we find acceptable, if at all.

In addition, clinical trials evaluating combination regimens such as the one we are proposing with the combination of bemnifosbuvir and a protease inhibitor are subject to additional costs, time and risks, including the requirement to sufficiently demonstrate the effect, if any, of each constituent component of the combination regimen to the satisfaction of the FDA or other regulatory authorities. For example, we expect that we will be required to conduct early stage clinical trials evaluating the safety of any newly discovered protease inhibitor candidate before we can conduct later stage clinical trials evaluating the combination of bemnifosbuvir with such protease inhibitor.

We have committed and plan to continue to commit significant financial and personnel resources to the development of bemnifosbuvir as a monotherapy, to the discovery of a protease inhibitor candidate to combine with bemnifosbuvir and to the combination of bemnifosbuvir and a protease inhibitor candidate for the treatment for COVID-19 (each, a "bemnifosbuvir COV19 product candidate"). If we are unable to successfully develop one or more bemnifosbuvir COV19 product candidates, we will have taken resources away from other development programs and may not be able to recuperate the resources dedicated to developing bemnifosbuvir COV19 product candidates, which could have a material adverse impact on our business. If we are unable to complete the SUNRISE-3 clinical trial on the timeline we anticipate or if data from our Phase 3 SUNRISE-3 clinical trial and other clinical trials are not supportive of further development or commercialization of one or more bemnifosbuvir COV19 product candidates, or the investor community otherwise has a negative reaction to any of the design of our clinical trial, expected time to complete our clinical trial or the clinical trial data, the demand for our common stock could decrease significantly, and the price of our common stock could decline substantially, which could result in significant losses for our stockholders.

Further, while we believe there is currently an urgent need for oral antiviral treatments for COVID-19, the longevity and extent of the ongoing COVID-19 pandemic is uncertain and it is unclear whether SARS-CoV-2 will become an endemic human coronavirus that may circulate in the human population after the current pandemic has subsided. If the pandemic were to dissipate, whether due to a significant decrease in the number or severity of new infections, the effectiveness of vaccines, the effectiveness of other treatment options, or otherwise, the need for treatments could decrease significantly. If the need for a new treatment decreases before or soon after commercialization of a bemnifosbuvir COV19 product candidate, if successfully developed and approved, our business would be adversely impacted.

A bemnifosbuvir COV19 product candidate, even if successfully developed and approved, is expected to face significant competition from other treatments and vaccines for COVID-19 which have been authorized or approved for use or are in development.

Many biotechnology and pharmaceutical companies have and are continuing to develop treatments for COVID-19 or vaccines against SARS-CoV-2, the virus that causes COVID-19. Many of these companies, which include large pharmaceutical companies, have greater resources for development and established commercialization capabilities.

Currently there are several vaccines and associated vaccine boosters approved or authorized for use for COVID-19 and there are therapeutics available for the treatment of COVID-19 including two oral antiviral therapies, Paxlovid™ developed by Pfizer Inc., and Lagevrio™ developed by Merck and Ridgeback Therapeutics, each of which are authorized for emergency use for high risk COVID-19 patients.

Additionally, Veklury, a nucleotide prodrug developed by Gilead Sciences, is approved for the treatment of COVID-19 in adults and pediatric patients who are hospitalized or if not hospitalized have mild to

moderate COVID-19 and are at high risk for progression to severe COVID-19, including hospitalization and death. Treatments in development for COVID-19 include GS-5245, an oral nucleoside prodrug, that is being developed by Gilead Sciences and is currently being evaluated in a randomized, double-blind placebo controlled Phase 3 clinical trial in non-hospitalized COVID patients who are at high risk of progression to hospitalization.

In addition to therapeutics, vaccines indicated for active immunization to prevent COVID-19 and vaccine "boosters," which are intended to extend the immunizing effect initiated with the administration of the initial vaccine have been approved or authorized for emergency use by the FDA. Vaccine manufacturers, including Pfizer and BioNTech SE and Moderna, Inc., are continuing to develop new vaccines and boosters that may have greater and longer immunizing effects against current and future variants of SARS-CoV-2.

Additional vaccines and therapeutics are in development by other pharmaceutical and biopharmaceutical companies. Other companies developing oral direct acting antivirals for treatment of COVID-19 include Enanta Pharmaceuticals, Inc., Shionogi & Co., Ltd., Pardes Biosciences, Inc., Junshi Biosciences, Jiangsu Simcere Pharmaceuticals, and SyneuRx.

Given the products currently approved or authorized for use as well as those in development by others, any treatment we may develop could face significant competition. If we are unable to develop a treatment that can be distinguished based on efficacy, safety, cost or other factors from the growing number of treatments for COVID-19 or if any treatment becomes the standard of care, can be administered more conveniently or at a lower cost, or any entity is more successful at commercializing an authorized or approved treatment, even if a bemnifosbuvir COV19 product candidate is approved, we may not be able to successfully commercialize such a product for the treatment of COVID-19, or compete with other treatments or vaccines, which would adversely impact our business and operations.

The COVID-19 pandemic may materially and adversely affect our business and financial results.

The global emergence of variants and subvariants of SARS-CoV-2 has resulted in an increasing number of infections, including breakthrough infections in persons who have been vaccinated against the infection. Travel bans, stay-at-home orders and other measures implemented by governments to reduce the transmission of COVID-19 in response to the initial outbreak of COVID-19 in 2020 caused widespread disruption in global business operations and economic activity. Future resurgences in cases may result in renewal of measures, many of which are currently relaxed, that are intended to reduce the spread of COVID-19. In response to the public health directives and to help minimize the risk of COVID-19 for our employees, we took and continue to maintain precautionary measures, including permitting work-from-home policies for all our employees. Many of our third-party collaborators, such as our CMOs, clinical research organizations ("CROs"), suppliers and others, took and continue to maintain similar precautionary measures. At times during the pandemic, these measures disrupted our business and delayed certain of our clinical programs and timelines. For example, in 2020 our hepatitis C virus clinical development program was paused when clinical trial sites closed due to COVID-19 precautions by the countries and medical facilities where the clinical trial was to be conducted. In 2023, we are planning to re-initiate HCV clinical trials.

The impact to our operations due to elongation or resurgence of the COVID-19 pandemic could be severe and could negatively affect our business, financial condition, and results of operations. For example, the recent relaxation of government lockdown measures in China has resulted in widespread outbreak of COVID-19. If continuing or new waves of COVID-19 infection disrupt business activities in China, our ability to source and manufacture critical components of our clinical trial material could be adversely impacted. To the extent that the COVID-19 pandemic adversely affects our business and financial results, it may also have the effect of heightening many of the other risk factors described in this "Risk Factors" section, such as those relating to our clinical trial timelines, our ability to enroll subjects for clinical trials and obtain materials that are required for the manufacture of our product candidates, and our ability to raise capital.

The evolution of the COVID-19 pandemic or occurrence of any other public health crises may materially and adversely affect our clinical trials.

As a result of the evolution of the COVID-19 pandemic or the occurrence of any other public health crises, we may experience additional disruptions that could severely impact our clinical trials, including but not limited to:

- delays or difficulties in enrolling patients in a clinical trial as a result of rapidly evolving treatment paradigms, particularly in the case of patients with COVID-19;
- patients that may not be able to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators, and clinical site staff, or the overwork of existing investigators and staff;
- diversion or prioritization of healthcare resources away from the conduct of clinical trials and towards the COVID-19 pandemic or other public health crises, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruptions or delays in preclinical studies due to restricted or limited operations at research and development laboratory facilities;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal, state or provincial governments, employers and others;
- the risk that participants enrolled in our non-COVID-19-related clinical trials will contract COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- limitations in employee resources that would otherwise be focused on the conduct of our clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials;
- interruption in global shipping that may affect the transport of clinical trial materials, such as investigational drug product and supplies;
- changes in local regulations as part of a response to the COVID-19 pandemic or other public health crises that may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees; and
- the refusal of the FDA or foreign regulatory authorities to accept data from clinical trials in these affected geographies.

The symptoms, progression, and transmission of COVID-19 resulting from infection with a particular variant or subvariant differ in multiple ways including severity of symptoms and rate of transmissibility. This rapid and continuing emergence of variants and the evolution of disease manifestation presents additional challenges for the conduct of our clinical trials in COVID-19 patients. For example, COVID-19 patients have presented with a wide range of symptoms and side effects, which may make it more difficult for clinical trial investigators to determine whether any adverse events observed in our clinical trials are related to bemnifosbuvir or are consistent with the underlying disease. Any increase in the severity or

incidence of adverse events deemed to be related to bemnifosbuvir or any combination regimen we seek to develop could delay or prevent its regulatory approval, which could have a material adverse effect on our business, financial condition and results of operations. In addition, efficacy and antiviral results from a COVID-19 clinical trial may be affected by, among other things, which variant or variants cause the infection, resulting transmissibility and severity of disease and related hospitalizations and deaths. As a result, response rates occurring throughout the duration of a clinical trial may be variable over time as the pandemic progresses.

Risks Related to Our Financial Condition and Capital Requirements

We have a limited operating history and no history of successfully developing or commercializing any approved antiviral products, which may make it difficult to evaluate the success of our business to date and to assess the prospects for our future viability.

We are a clinical-stage biopharmaceutical company. Our operations to date have been limited to financing and staffing our company, developing our technology, and identifying and developing our product candidates. Our prospects must be considered in light of the uncertainties, risks, expenses and difficulties frequently encountered by biopharmaceutical companies in their early stages of operations. We have not yet demonstrated an ability to complete any late-stage or pivotal clinical trials, obtain marketing approval, manufacture a product at commercial-scale, or conduct sales and marketing activities necessary for successful product commercialization, or have third parties to do these activities on our behalf. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing, obtaining marketing approval for and commercializing antiviral therapies.

In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown obstacles. For example, due to changes in the COVID-19 landscape, we discontinued our Phase 3 MORNINGSKY trial in December 2021 and have only recently initiated a subsequent Phase 3 clinical trial, SUNRISE-3, evaluating bemnifosbuvir for the treatment of high risk outpatients with mild or moderate COVID-19. The primary endpoint of the SUNRISE-3 trial is all cause hospitalization or death through day 29 in the population of enrolled patients who receive only bemnifosbuvir or placebo without co-administration of the local standard care therapeutic. Our current study design and sample size contemplates that the rate of hospitalization in the placebo cohort will be at least 4%. If the actual rate of hospitalization in the placebo cohort of patients is less, the sample size and number of patients enrolling overall in the trial may need to be increased. This would make the trial more difficult to complete, if at all, and the time and cost for completion of the trial would be expected to increase. As the COVID-19 landscape has evolved, rates of testing, diagnosis and hospitalization for COVID-19 have and continue to vary substantially. Reported rates of hospitalization in many geographic regions have and may continue to fluctuate significantly including being reported below 4% for the overall patient population in specific regions.

If we successfully develop and obtain approval of any product candidate, we will need to transition from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in this transition.

As we continue to build our business, we expect our financial condition and operating results may fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. For example, the decision by Roche to terminate the Roche License Agreement also terminated Roche's obligation, after February 10, 2022, the effective date of the termination of the Roche License Agreement, to share with us costs associated with the development of bemnifosbuvir for the treatment of COVID-19.

Additionally, as a further result of the termination of the Roche License Agreement, we will not receive any other revenue from Roche beyond the upfront payment we received in 2020 and the milestone payment we received in 2021. Accordingly, you should not rely upon the results included in this report or reports for any other particular prior quarterly or annual period as indications of future operating performance.

We have incurred significant operating expenses since inception and expect to incur significant additional operating expenses for the foreseeable future. We have no products that have generated any commercial revenue and we do not expect to maintain profitability in 2022 and for the foreseeable future.

We have incurred significant operating expenses since our inception. For the year ended December 31, 2022 and the year ended December 31, 2021, our operating expenses were $130.7 million and $213.0 million, respectively. In 2021, as a result of the termination by Roche of the Roche License Agreement, which resulted in the recognition of revenue for accounting purposes associated with the deferred revenue balance associated with upfront payment and the milestone payment we received from Roche, we recorded operating income for the year ended December 31, 2021. For the year ended December 31, 2022, we did not record any operating income and we do not expect to realize operating income in 2023 or for the foreseeable future.

We have not commercialized any products and have never generated any revenue from product sales. We have devoted almost all of our financial resources to research and development, including our clinical trials and preclinical development activities. We expect to continue to incur significant additional operating expenses and to incur operating losses for the foreseeable future as we seek to advance product candidates through clinical development, continue preclinical development, expand our research and development activities, discover or acquire and develop product candidates, including any product candidate we may seek to combine with bemnifosbuvir for the potential treatment of COVID-19, complete preclinical studies and clinical trials, seek regulatory approval and, if we receive regulatory approval, commercialize our products.

In order to obtain the FDA's or a foreign regulatory authority's approval to market any product candidate in the US or abroad, respectively, we must submit to the FDA an NDA or similar application to the foreign regulatory authority demonstrating to the FDA's or foreign regulatory authority's satisfaction that the product candidate is safe and effective for its intended use(s). This demonstration requires significant research and extensive data from animal tests, which are referred to as nonclinical or preclinical studies, as well as human tests, which are referred to as clinical trials.

Furthermore, the costs of advancing product candidates into each succeeding clinical phase tend to increase substantially over time. The total costs to advance any of our product candidates to marketing approval in even a single jurisdiction would be substantial and difficult to accurately predict. Because of the numerous risks and uncertainties associated with the development of drug products, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to begin generating revenue from the commercialization of products or again achieve profitability. As we advance clinical development activities, particularly our Phase 3 SUNRISE-3 clinical trial for the treatment of high risk outpatients with mild or moderate COVID-19 and our Phase 2 clinical trial evaluating the combination of bemnifosbuvir and ruzasvir for the treatment of HCV, we expect our expenses will increase substantially. Additionally, our expenses will also increase substantially if or as we:

- initiate clinical trials of a potential bemnifosbuvir combination regimen for the treatment of patients with COVID-19;
- continue to discover and develop additional product candidates;
- seek regulatory and marketing approvals for product candidates that successfully complete clinical trials, if any;
- establish manufacturing and supply chain capacity sufficient to provide commercial quantities of any product candidates for which we may obtain marketing approval, if any;
- establish a sales, marketing, internal systems and distribution infrastructure to commercialize any products for which we may obtain regulatory approval, if any, in geographies in which we plan to commercialize our products ourselves or with co-promotion collaborators;
- maintain, expand, protect and enforce our intellectual property portfolio;

- hire additional staff, including clinical, scientific, technical, regulatory, operational, financial, commercial and support personnel, to execute our business plan and support our product development and potential future commercialization efforts;
- more extensively utilize external vendors for support with respect to research, development, manufacturing, commercialization, regulatory, pharmacovigilance and other functions;
- acquire or in-license commercial products or additional product candidates and technologies;
- make milestone, royalty or other payments under the license agreement we entered into in December 2021 with MSD International GmbH, an affiliate of Merck & Co, Inc. ("Merck") with respect to the development and commercialization of ruzasvir for the treatment of HCV;
- make upfront, milestone, royalty or other payments in connection with any future in-license agreements relating to other product candidates; and
- incur continuing and increasing legal, accounting and other expenses in operating our business as a public company.

Furthermore, our ability to successfully develop, commercialize and license any products and generate product revenue is subject to substantial additional risks and uncertainties. Each of our product candidates and any future product candidate we may discover, license or otherwise acquire, will require additional preclinical and/or clinical development, regulatory approval in not less than one jurisdiction, the securing of manufacturing supply, capacity, distribution channels and expertise, the use of external vendors, the building of a commercial organization, substantial investment and significant marketing efforts before we generate any revenue from product sales. As a result, we expect to continue to use cash for operating activities and incur operating expenses and operating losses for the foreseeable future. The use of cash and incurrence of operating expenses and operating losses has had, and we expect will continue to have, an adverse effect on our working capital.

The amount of future expenses or losses and our ability to achieve or maintain profitability in future years, if ever, are uncertain. We have no products that have generated any commercial revenue, do not expect to generate revenues from the commercial sale of products in the foreseeable future, and might never generate revenues from the sale of products. Our ability to generate product revenue and maintain profitability will depend on, among other things, successful completion of the clinical development of our product candidates; obtaining necessary regulatory approvals from the FDA and foreign regulatory authorities; establishing manufacturing and sales capabilities; market acceptance of our products, if approved, and establishing marketing infrastructure or otherwise arranging to commercialize our product candidates for which we obtain approval; and raising sufficient funds to finance our activities. We might not succeed at any of these undertakings. If we are unsuccessful at some or all of these undertakings, our business, prospects, and results of operations may be materially adversely affected.

We will require substantial additional financing, which may not be available on acceptable terms, or at all. A failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our product development or commercialization efforts.

Since inception, we have incurred substantial operating expenses. We expect to incur substantial expenses in connection with our current and planned business activities, particularly the conduct of the Phase 3 SUNRISE-3 clinical trial for the treatment of high risk outpatients with mild or moderate COVID-19 and our Phase 2 clinical trial evaluating the combination of bemnifosbuvir and ruzasvir for the treatment of HCV. Additionally, we anticipate that we will incur substantial expenses in connection with the development of a combination bemnifosbuvir COV19 product candidate and in connection with the discovery, acquisition and development of other product candidates.

We will continue to need additional capital to fund future clinical trials and preclinical development, which we may raise through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or other sources. Additional sources of financing might not be available on favorable terms, if at all. If we do not succeed in raising additional funds on acceptable terms, we might be unable to initiate or complete planned clinical trials or seek regulatory approvals of any of our product candidates from the FDA, or any foreign regulatory authorities,

and could be forced to discontinue product development. In addition, attempting to secure additional financing could divert the time and attention of our management from day-to-day activities and may harm our product candidate development efforts.

Based on our current operating plan, we believe that our cash and cash equivalents as of December 31, 2022 will be sufficient to fund our operating expenses and capital expenditure requirements into 2026. This estimate is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. We will require significant additional funds in order to launch and commercialize our current and any future product candidates to the extent that such launch and commercialization are not the responsibility of a collaborator. In addition, other unanticipated costs may arise in the course of our development efforts. Because the design and outcome of our planned and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and, if approved, commercialization of any product candidate we develop.

Our future capital requirements depend on many factors, including but not limited to:

- the timing of and costs associated with discovery, license or acquisition of a protease inhibitor or another direct acting antiviral product candidate to combine with bemnifosbuvir and develop for the treatment of patients with COVID-19;
- the scope, progress, results and costs of our preclinical studies and clinical trials, in particular our Phase 3 SUNRISE-3 clinical trial;
- the timing of, and the costs involved in, obtaining marketing approvals for our current and future product candidates in regions where we choose to commercialize any products;
- the number of future product candidates and potential additional indications that we may pursue and their development requirements;
- the stability, scale, yield and cost of manufacturing our product candidates for clinical trials, in preparation for regulatory approval and in preparation for commercialization;
- the costs of commercialization activities for any approved product candidate 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;
- revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval;
- the costs, timing and changes in pharmaceutical pricing and reimbursement infrastructure which are anticipated in connection with the enactment of the Inflation Reduction Act of 2022 ("IRA") and other legislation and regulations that may be subsequently enacted;
- subject to receipt of regulatory approval, revenue, if any, received from commercial sales for any approved indications for any of our product candidates;
- our ability to compete with other therapies in the indications we target;
- the extent to which we in-license or acquire rights to products, product candidates or technologies in addition to ruzasvir;
- the continued growth of our headcount and associated costs as we expand our research and development capabilities and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications and maintaining and protecting our intellectual property rights, including enforcing and defending intellectual property-related claims; and
- the continued costs of operating as a public company.

Currently, we do not have any committed external source of funds or other support and we cannot be certain that additional funding will be available on acceptable terms, or at all. The COVID-19 pandemic,

including the evolution of new and existing variants of COVID-19, and geopolitical events, including civil or political unrest (such as the ongoing war between Ukraine and Russia), have resulted in a significant disruption of global financial markets. In addition, recent or future market volatility, increased inflation and higher interest rates, if sustained, may increase our cost of financing and may restrict our access to potential sources of future liquidity. If we are unable to raise additional capital in sufficient amounts, on terms acceptable to us, or on a timely basis, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates or other research and development initiatives.

We have not generated any revenue from product sales and may not be able to achieve profitability.

Due to the recognition of revenue for accounting purposes of certain payments we received under the terminated Roche License Agreement, we recognized operating income for the year ended December 31, 2021. However, following the termination of the Roche License Agreement, we have received no incremental payments from Roche or any other third party that were recognized as revenue. As a result we incurred an operating loss in the amount of $130.7 million for the year ended December 31, 2022. Our ability to achieve and sustain future profitability depends upon our ability to generate revenue from product sales. Other than from the Roche License Agreement, we have not generated any revenue and do not expect to generate product revenue unless or until we successfully complete clinical development and obtain regulatory approval of, and then successfully commercialize, at least one of our product candidates. Our product candidates are in varying stages of development, which is expected to necessitate additional preclinical studies in some cases and in all cases will require additional clinical development as well as regulatory review and approval, substantial investment, access to sufficient commercial manufacturing capacity and significant marketing efforts before we can generate any revenue from product sales. Currently, we do not anticipate generating revenue from product sales for at least the next several years. Our ability to generate revenue depends on a number of factors, including, but not limited to:

- completion of our Phase 3 SUNRISE-3 clinical trial for the treatment of high risk outpatients with mild to moderate COVID-19 on the timeline we anticipate and timely initiation and completion of other clinical trials including the Phase 2 trial evaluating the combination of bemnifosbuvir and ruzasvir for the treatment of HCV and potentially initiation and completion of clinical trials evaluating a bemnifosbuvir combination regimen for the treatment of COVID-19, preclinical studies and other future clinical trials of other product candidates, each of which may be significantly slower or more costly than we currently anticipate and will depend substantially upon the performance of third-party contractors;
- our ability to complete additional IND enabling studies and successfully submit INDs, CTAs or comparable applications to allow us to initiate clinical trials for any other product candidates;
- whether we are required by the FDA or similar foreign regulatory authorities to conduct additional clinical trials or other studies beyond those planned to support the approval and commercialization of our product candidates or any future product candidates;
- our ability to demonstrate to the satisfaction of the FDA or similar foreign regulatory authorities the safety and efficacy of our product candidates or any future product candidates;
- the prevalence, duration and severity of potential side effects or other safety issues experienced with our product candidates or future product candidates, if any;
- the timely receipt of necessary marketing approvals from the FDA or similar foreign regulatory authorities;
- the availability, actual and perceived advantages and relative cost, convenience, safety and efficacy of any bemnifosbuvir COV19 product candidate, we may be able to commercialize, compared to other COVID-19 therapies as well as the accuracy and sufficiency of clinical evidence supporting its performance;

- the willingness of physicians, operators of clinics and patients to conduct or participate in clinical trials evaluating our product candidates and, if successfully developed, to utilize or adopt any of our product candidates or future product candidates that may be approved as antiviral therapies;
- our ability and the ability of third parties with whom we contract to manufacture adequate clinical and commercial supplies of our current or future product candidates, remain in good standing with regulatory authorities and develop, validate and maintain commercially viable manufacturing processes that are compliant with current good manufacturing practices ("cGMP") or similar requirements outside the US;
- our ability to successfully establish a commercial strategy and thereafter commercialize our current or future product candidates, in the US and internationally, if approved for marketing, reimbursement, sale and distribution in such countries and territories, whether alone or in collaboration with others; and
- our ability to establish, maintain, protect and enforce intellectual property rights in and to our product candidates or any future product candidates.

Many of the factors listed above are beyond our control, and could cause us to experience significant delays or prevent us from obtaining regulatory approvals or commercializing our product candidates. Even if we are able to commercialize our product candidates, we may not be able to maintain profitability after generating product sales or meet outside expectations for our profitability. If we are unable to achieve or sustain profitability or to meet outside expectations for our profitability, the value of our common stock will be materially adversely affected. In addition, if we are unable to generate sufficient revenue through the sale of any products, we may be unable to continue operations.

Our ability to use our net operating loss carryforwards and other tax attributes to offset taxable income may be subject to certain limitations.

As of December 31, 2022, we had US federal net operating loss carryforwards ("NOLs"), of $19.4 million, which may be available to offset future taxable income, if any, of which $0.4 million begin to expire in 2034 and of which $19.0 million do not expire but are limited in their usage (for taxable years beginning after December 31, 2022) to an annual deduction equal to 80% of annual taxable income. In addition, as of December 31, 2022, we had state NOLs of $30.0 million, which may be available to offset future taxable income, if any, and begin to expire in 2042. During the year ending December 31, 2021, we utilized each of federal and state NOLs of approximately $52.8 million and $52.6 million, respectively, and federal and state research and development credit carryforwards of $0.7 million and $0.3 million, respectively.

In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended ("Code"), a corporation that undergoes an "ownership change," generally defined as a greater than 50% change by value in its equity ownership over a three-year period, is subject to limitations on its ability to utilize its pre-change NOLs and its research and development credit carryforwards to offset future taxable income. Our NOLs and research and development credit carryforwards may be subject to limitations arising from previous ownership changes, and if we undergo an ownership change, our ability to utilize NOLs (to the extent not previously utilized) and research and development credit carryforwards could be further limited by Sections 382 and 383 of the Code.

For the year ended December 31, 2021, we have completed a Section 382 study, the results of which indicated that no ownership shift occurred during such period. However, this conclusion could be challenged by tax authorities. In addition, future changes in our stock ownership, some of which might be beyond our control, could result in an ownership change under Sections 382 and 383 of the Code. For these reasons, we may not be able to utilize existing NOLs or research and development credit carryforwards or net operating losses and research and development credits that may be generated in the future. We are in the process of completing a Section 382 study for the year ended December 31, 2022.

We may delay, suspend or terminate the development of a product candidate at any time if we believe the perceived market or commercial opportunity does not justify further investment or for other strategic business, financial or other reasons, which could materially harm our business and adversely affect our stock price.

Even if the results of preclinical studies and clinical trials that we have conducted or may conduct in the future may support further development of one or more of our product candidates, we may delay, suspend or terminate the future development of a product candidate at any time for strategic, business, financial or other reasons, including the determination or belief that the emerging profile of the product candidate is such that it may not receive regulatory approvals in key markets, gain meaningful market acceptance, otherwise provide any competitive advantages in its intended indication or market or generate a significant return to stockholders. In February 2023, after advancing AT-752 to Phase 2 clinical trial, we suspended the clinical development of AT-752 for the treatment and prophylaxis of dengue. This action was taken due to the anticipated long timelines and other challenges associated with the clinical development of an antiviral for the treatment of dengue. We have also recently terminated our efforts to discover a product candidate for the treatment of RSV. This action was taken to facilitate enhanced focus of our management team and resources for therapeutic indications where our programs are more advanced. These actions and any other similar delays, suspensions or terminations of other clinical programs or product candidates could materially harm our business, results of operations or financial condition.

Risks Related to the Discovery, Development, Preclinical and Clinical Testing, Manufacturing and Regulatory Approval of Our Product Candidates

Our business is highly dependent on our ability to develop one or more bemnifosbuvir COV19 product candidates. If we are not successful in developing a bemnifosbuvir COV19 product candidate, our business will be harmed. Our business is also highly dependent on the success of our other most advanced product candidates, including the combination of bemnifosbuvir and ruzasvir for the treatment of HCV, which will require significant additional clinical testing before we can seek regulatory approval and potentially launch commercial sales. If these product candidates fail in clinical development, do not receive regulatory approval or are not successfully commercialized, or are significantly delayed in doing so, our business will be harmed.

A substantial portion of our business and future success depends on our ability to develop, obtain regulatory approval for and successfully commercialize one or more bemnifosbuvir COV19 product candidates and the combination of bemnifosbuvir and ruzasvir for the treatment of HCV. We currently have no products that are approved for commercial sale and have not completed the development of any of our product candidates, and we may never be able to develop marketable products. During the near term we expect that a substantial portion of our efforts and expenditures will continue to be devoted to developing a potential bemnifosbuvir COV19 product candidate. Among other things, this effort will require the successful completion of our Phase 3 SUNRISE-3 clinical trial for the treatment of high risk outpatients with mild to moderate COVID-19 and additional nonclinical and clinical development and the incurrence of expenses related to discovering, acquiring or in-licensing a drug or drug candidate to combine with bemnifosbuvir for the treatment of COVID-19. COVID-19, while currently a global pandemic, is unpredictable and therapies, including any bemnifosbuvir COV19 product candidate, may be adversely impacted up to the point of obsolescence by the emergence of new variants or subvariants as well as by the development and authorization and approval of new vaccines, vaccine boosters and therapeutics. Additionally, we expect that a substantial portion of our efforts and expenditures over the next few years will be devoted to developing the combination of bemnifosbuvir and ruzasvir for the treatment of HCV which will require additional clinical development, management of clinical, medical affairs and manufacturing activities, obtaining regulatory approvals in multiple jurisdictions, securing of manufacturing supply, building of a commercial organization, substantial investment and significant marketing efforts. We cannot be certain that any of our current or future product candidates will be successful in clinical trials, receive regulatory approval or be successfully commercialized even if we receive regulatory approval. Further, our development of any product candidate may be delayed or suspended, which may affect our ability to successfully commercialize such product candidate.

If our competitors develop products to treat diseases and, if applicable, specified patient populations which our current or future product candidates are being developed to treat, before we are able to successfully develop a product candidate, or if our competitors develop any products that are superior to our product candidates, our potential market share could become smaller or non-existent. Even if we receive approval to market any product candidate, we cannot be certain that our product candidates will be as or more effective than other commercially available alternatives, successfully commercialized or widely accepted in the marketplace. Nor can we be certain that, if approved, the safety and efficacy profile of any product will be consistent with the results observed in clinical trials, or in the case of a bemnifosbuvir COV19 product candidate, that it will demonstrate efficacy against continuing mutations of the SARS-COV-2 virus, the causative agent of COVID-19. If we are not successful in the clinical development of a bemnifosbuvir COV19 product candidate or our other most advanced product candidates, the required regulatory approvals for these product candidates are not obtained, there are significant delays in the development or approval of these product candidates, or any approved products are not commercially successful, our business, financial condition and results of operations may be materially harmed.

The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, expensive, time-consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be seriously harmed.

We are not permitted to commercialize, market, promote or sell any product candidate in the US without obtaining marketing approval from the FDA. Foreign regulatory authorities impose similar requirements. The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved and the disease or condition for which the product candidate is intended, particularly with respect to COVID-19, which continues to evolve rapidly. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application.

Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. We have not submitted an NDA for, or obtained regulatory approval of, any product candidate. We must complete additional preclinical or nonclinical studies and clinical trials to demonstrate the safety and efficacy of our product candidates in humans to the satisfaction of the regulatory authorities before we will be able to obtain these approvals, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval. Applications for our product candidates could fail to receive regulatory approval for many reasons, including but not limited to the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design, implementation or interpretation of results of our clinical trials;
- the FDA or comparable foreign 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 of our products;
- the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- we may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate's clinical and other benefits outweigh its safety risks;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the US or elsewhere;

- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; 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 for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which would seriously harm our business. In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may impose significant limitations in the form of narrow indications, warnings, or a Risk Evaluation and Mitigation Strategy ("REMS") or similar risk management measures. Regulatory authorities may not approve the price we intend to charge for products we may develop, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could seriously harm our business.

Clinical development, including enrollment of patients in clinical trials, is an expensive, lengthy and uncertain process. We may encounter substantial delays and costs in our clinical trials, or may not be able to conduct or complete our clinical trials on the timelines we expect, if at all.

Before obtaining marketing approval from the FDA or other comparable foreign regulatory authorities for the sale of our product candidates, we must complete preclinical development and extensive clinical trials to demonstrate the safety and efficacy of our product candidates. Clinical testing is expensive, time-consuming and subject to uncertainty. A failure of one or more clinical trials can occur at any stage of the process, such as the failure in October 2021 of bemnifosbuvir to meet the primary endpoint in the overall patient population in the Phase 2 MOONSONG clinical trial. The outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later clinical trials. This may be particularly true in the development of therapeutics for the treatment of COVID-19, including our development of bemnifosbuvir COV19 product candidates, where the evolution of the virus and disease have occurred at such a rapid rate that product candidates in development have the potential to become obsolete before clinical development is completed. Moreover, preclinical and clinical data, particularly the analysis of exploratory endpoints and analysis of data derived from patient subgroups, such as the data from the MORNINGSKY study upon which we have relied to continue clinical development, are often susceptible to varying interpretations, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their drugs. To date, we have not completed any late-stage or pivotal clinical trials for any of our product candidates. We cannot guarantee that any of our planned or ongoing clinical trials will be initiated or conducted as planned or completed on schedule, if at all. We also cannot be sure that submission of any future IND or similar application will result in the FDA or other regulatory authority, as applicable, allowing future clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, issues may arise that could cause regulatory authorities to suspend or terminate such clinical trials. A failure of one or more clinical trials can occur at any stage of testing, and our future clinical trials may not be successful. Events that may prevent successful or timely initiation or completion of clinical trials include but are not limited to:

- inability to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation or continuation of clinical trials;
- delays in reaching a consensus with regulatory authorities on study design or implementation of the clinical trials;
- delays or failure in obtaining regulatory authorization to commence a trial;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among CROs and clinical trial sites;
- delays in identifying, recruiting and training suitable clinical investigators;

- delays in obtaining required IRB or ethics committee approval or positive opinion at each clinical trial site;
- delays in recruiting, screening and enrolling a suitable number and diversity of patients to participate in our clinical trials;
- delays in manufacturing, testing, releasing, validating or importing/exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing;
- insufficient or inadequate supply or quality of product candidates or other materials necessary for use in clinical trials, or delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for clinical trials;
- imposition of a temporary or permanent clinical hold by regulatory authorities for a number of reasons, including after review of an IND or amendment or equivalent foreign application or amendment; as a result of a new safety finding that presents unreasonable risk to clinical trial participants; or a negative finding from an inspection of our clinical trial operations or study sites;
- developments on trials conducted by competitors for related technology that raises FDA or foreign regulatory authority concerns about risk to patients of the technology broadly, or if the FDA or a foreign regulatory authority finds that the investigational protocol or plan is clearly deficient to meet its stated objectives;
- delays caused by patients withdrawing from clinical trials or failing to return for post-treatment follow-up, including due to the COVID-19 pandemic or political unrest and war, including the current conflict between the Ukraine and Russia and any escalation or spillover into additional regions;
- difficulty collaborating with patient groups and investigators;
- failure by our CROs, other third parties or us to adhere to clinical trial protocols; failure to perform in accordance with the FDA's or any other regulatory authority's GCPs, or applicable regulatory guidelines in other countries;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits, or occurrence of adverse events in trial of the same class of agents conducted by other companies;
- changes to the clinical trial protocols;
- subjects enrolled in our clinical trials or clinical sites deviating from the clinical trial protocol or dropping out of a trial;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- selection of clinical endpoints that require prolonged periods of observation or analyses of resulting data;
- the cost of clinical trials of our product candidates being greater than we anticipate;
- clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon development of such product candidates;

- transfer of manufacturing processes to larger-scale facilities operated by a CMO and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process; and
- third parties being unwilling or unable to satisfy their contractual obligations to us.

In addition, events, occurrences and disruptions caused by the continuing evolution of COVID-19 may increase the likelihood that we encounter difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials. In particular, the rate of incidence, testing and diagnosis of COVID-19, changes in the standard of care for the treatment of COVID-19, which is rapidly evolving due to the mutation of the virus, rapidly increasing knowledge being obtained by healthcare providers, rates and durability of vaccines, and availability of an increasing number of therapeutic options, may impact the successful completion of our Phase 3 SUNRISE-3 clinical trial and other COVID-19-related clinical trials we may initiate.

Any inability to successfully complete our Phase 3 SUNRISE-3 clinical trial or the completion of any other planned clinical trials we may initiate could result in additional costs to us or impair our ability to generate revenue from product sales. In addition, if we make manufacturing or formulation changes to our product candidates, we may be required to or we may elect to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which any approved products have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may seriously harm our business.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the DSMB for such trial, or by the FDA or any other regulatory authority, or if the IRBs of the institutions in which such trials are being conducted suspend or terminate the participation of their clinical investigators and sites subject to their review. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Further, conducting clinical trials in foreign countries, as we are currently doing and otherwise expect to continue doing for other product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or 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.

Delays in the completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate product revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Any delays to our clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize our product candidates and our competitors may be able to bring products to market before we do, which could

significantly reduce the commercial viability of our product candidates. Any of these occurrences may harm our business, financial condition and prospects significantly.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the European Union ("EU") recently evolved. The EU CTR which was adopted in April 2014 and repeals the EU Clinical Trials Directive ("Clinical Trial Directive"), became applicable on January 31, 2022. While the Clinical Trials Directive required a separate CTA to be submitted in each member state, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials whose CTA was made under the Clinical Trials Directive before January 31, 2022, the Clinical Trials Directive will continue to apply on a transitional basis for three years. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the Clinical Trials Directive 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. Through January 31, 2023, submissions of CTAs that we made in connection with each of our SUNRISE-3 Phase 3 clinical trial and our Phase 2 HCV clinical trial were made using the Clinical Trial Directive. We have only begun submitting CTAs under the CTR since February 1, 2023. Our experience with submissions under the CTR is limited. Compliance with the CTR requirements by us and our third-party service providers, such as clinical research organizations ("CROs"), may impact our developments plans.

It is currently unclear to what extent the UK will seek to align its regulations with the EU. The UK regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into UK law, through secondary legislation). On January 17, 2022, the UK Medicines and Healthcare products Regulatory Agency ("MHRA") launched an eight-week consultation on reframing the UK legislation for clinical trials. The consultation closed on March 14, 2022 and aims to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The outcome of the consultation is being closely watched and will determine whether the UK chooses to align with the CTR or diverge from it to maintain regulatory flexibility. A decision by the UK not to closely align its regulations with the new approach that has been adopted in the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may also be impacted.

We intend to develop certain of our product candidates in combination with other therapies, which exposes us to additional risks.

Combination therapies are commonly used for the treatment of viral infections. We are currently planning to develop combination therapies for the treatment of COVID-19 and HCV. Developing combination therapies exposes us to additional clinical risks, such as the requirement that we demonstrate the safety and efficacy of each active component of any combination regimen we may develop.

For the treatment of COVID-19 patients, in addition to our development of bemnifosbuvir as a monotherapy, we anticipate that we will develop a combination product consisting of bemnifosbuvir and an investigational protease inhibitor that is currently the subject of internal discovery efforts. For the treatment of HCV, we are currently pursuing development of bemnifosbuvir in combination with ruzasvir, a product candidate that has not yet been approved for marketing by the FDA or similar foreign regulatory

authorities. We may not be able to market and sell any product candidate we develop in combination with any such unapproved therapies that do not ultimately obtain marketing approval.

If the FDA or similar foreign regulatory authorities do not approve these other combination agents or revoke their approval thereof, or if safety, efficacy, manufacturing, or supply issues arise with the drugs or biologics we choose to evaluate in combination with our product candidates, we may be unable to obtain approval of or market our product candidates for combination therapy regimens.

Additionally, if the third-party manufacturers of therapies or therapies in development used in combination with our product candidates are unable to produce sufficient quantities for clinical trials or for commercialization of our product candidates, or if the cost of combination therapies are prohibitive, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

Our product candidates may be associated with serious adverse events, undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential or result in significant negative consequences.

Adverse events or other undesirable side effects caused by our product candidates could cause us, our collaborators, any DSMB for a trial, or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities.

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries, and discomforts, to their study doctor. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. It is possible that as we test our product candidates in larger, longer and more extensive clinical trials, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in previous trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. Many times, side effects are only detectable after investigational products are tested in large-scale clinical trials or, in some cases, after they are made available to patients on a commercial scale following approval.

If any serious adverse events occur, clinical trials or commercial distribution of any product candidates or products we develop could be suspended or terminated, and our business could be seriously harmed. Treatment-related side effects could also affect patient recruitment and the ability of enrolled patients to complete the trial or result in potential liability claims. Regulatory authorities could order us to cease further development of, deny approval of, or require us to cease selling any product candidates or products for any or all targeted indications. If we are required to delay, suspend or terminate any clinical trial or commercialization efforts, the commercial prospects of such product candidates or products may be harmed, and our ability to generate product revenues from them or other product candidates that we develop may be delayed or eliminated. Additionally, if one or more of our product candidates receives marketing approval and we or others later identify undesirable side effects or adverse events caused by such products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may suspend, limit or withdraw approvals of such product, or seek an injunction against its manufacture or distribution;
- regulatory authorities may require additional warnings on the label, including “boxed” warnings, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- we may be required to change the way the product is administered or conduct additional clinical trials or post-approval studies;
- we may be required to create a REMS or similar risk management measures which could include a medication guide outlining the risks of such side effects for distribution to patients;
- we may be subject to fines, injunctions or the imposition of criminal penalties;

- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could seriously harm our business, financial condition and results of operations.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. The enrollment of patients depends on many factors, including but not limited to:

- the patient eligibility criteria defined in the protocol;
- the size of the target disease population and rates of diagnostic testing among the target disease population;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating;
- our ability to obtain and maintain patient consents;
- the risk that patients enrolled in clinical trials will drop out of the trials before trial completion; and
- other factors outside of our control, such as the COVID-19 pandemic which has, among other things, created substantial burdens on healthcare providers who may be required to prioritize immediate critical patient care over clinical research and political unrest and war, including the current conflict between the Ukraine and Russia and any escalation or spillover into additional regions.

In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates or similar areas, and this competition may reduce the number and types of patients available to us because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. For example, we are aware of a number of clinical trials sponsored by our potential competitors that are evaluating oral antivirals for the treatment of high risk outpatients with mild to moderate COVID-19, the same patient population that we are seeking to enroll in SUNRISE-3. Since the number of qualified clinical investigators is limited, it is possible that we will conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites.

Delays in patient enrollment as a result of competition, or in the case of COVID-19 in particular, evolution of the disease and treatment paradigms as well as rates of testing and diagnoses or for other reasons may result in increased costs or may affect the timing or outcome of our ongoing and planned clinical trials, which could prevent completion or commencement of these trials and adversely affect our ability to advance the development of our product candidates.

A Fast Track Designation by the FDA may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.

If a product candidate is intended for the treatment of a serious or life-threatening condition and the product candidate demonstrates the potential to address unmet medical needs for such condition, the product candidate sponsor may apply for Fast Track Designation. The sponsor of a product candidate that has received Fast Track Designation may have opportunities for more frequent interactions with the FDA review team during product development and, once a New Drug Application ("NDA") is submitted, the NDA may be eligible for priority review. An NDA for a Fast Track product candidate may also be eligible for rolling review, where the FDA may consider review of sections of the NDA on a rolling basis before the complete NDA is submitted.

The FDA has broad discretion whether or not to grant Fast Track Designation to any particular product candidate. As a result, we may seek such Fast Track Designation for other product candidates, including bemnifosbuvir COV19 product candidates, but cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Many product candidates that have received Fast Track Designation have nevertheless failed to obtain approval.

We currently conduct clinical trials, and may in the future choose to conduct additional clinical trials, of our product candidates in sites outside the US, and the FDA may not accept data from trials conducted in foreign locations.

We currently conduct, and expect in the future to conduct, clinical trials outside the US for our product candidates. The acceptance of study data from clinical trials conducted outside the US or another jurisdiction by the FDA or comparable foreign regulatory authority 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 US, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the US population and US 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, if the study was not otherwise subject to an IND, the FDA will not accept the data as support for an application for marketing approval unless the study was 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 US 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.

In addition, there are risks inherent in conducting clinical trials in multiple jurisdictions, inside and outside of the US, such as:

- regulatory and administrative requirements of the jurisdiction where the trial is conducted that could burden or limit our ability to conduct our clinical trials;
- foreign exchange fluctuations;
- manufacturing, customs, shipment and storage requirements;

- cultural differences in medical practice and clinical research; and
- the risk that the patient populations in such trials are not considered representative as compared to the patient population in the target markets where approval is being sought.

Interim, "topline" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or top-line data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. Consequently, the top-line or preliminary data that we report may differ from final results reported from the same studies, or different conclusions or considerations may qualify such preliminary or topline data, once additional data have been received and fully evaluated. Top-line and preliminary data also remain subject to audit and verification procedures that may result in the final results being materially different from the preliminary or topline data we previously published. As a result, top-line data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may subsequently complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Adverse differences between preliminary or interim data and final results could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general.

In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the interim, top-line, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

We may not be successful in our efforts to identify and successfully develop additional product candidates.

Part of our strategy involves identifying novel product candidates. For example, we are currently engaged in internal efforts to discover a protease inhibitor product candidate that we may be able to combine with bemnifosbuvir for the treatment of COVID-19. These efforts and any subsequent discovery efforts we initiate to identify other novel product candidates may fail to yield product candidates for clinical development for a number of reasons, including those discussed in these risk factors and also:

- we may not be able to assemble sufficient resources to acquire or discover additional product candidates;
- competitors may develop alternatives that render our potential product candidates obsolete or less attractive;
- potential product candidates we develop may nevertheless be covered by third-parties' patent or other intellectual property or exclusive rights;

- potential product candidates may, on further study, be shown to have harmful side effects, toxicities or other characteristics that indicate that they are unlikely to be products that will receive marketing approval or achieve market acceptance, if approved;
- potential product candidates may not be effective in treating their targeted diseases or symptoms;
- the market for a potential product candidate may change so that the continued development of that product candidate is no longer reasonable;
- a potential product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or
- the regulatory pathway for a potential product candidate is highly complex and difficult to navigate successfully or economically.

If we are unable to identify and successfully develop and commercialize additional suitable product candidates, this would adversely impact our business strategy and our financial position.

We may focus on potential product candidates that may prove to be unsuccessful and we may have to forego opportunities to develop other product candidates that may prove to be more successful.

We may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful, or to license or purchase a marketed product that does not meet our financial expectations. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases that may later prove to have greater commercial potential.

Furthermore, we have limited financial and personnel resources and are placing significant focus on the development of our lead product candidates, particularly bemnifosbuvir COV19 product candidates and bemnifosbuvir in combination with ruzasvir for the treatment of HCV, and as such, we may forgo or delay pursuit of opportunities with other future product candidates that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and other future product candidates for specific indications may not yield any commercially viable future product candidates. If we do not accurately evaluate the commercial potential or target market for a particular future product candidate, we may relinquish valuable rights to those future product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such future product candidates.

We may attempt to secure FDA approval of certain product candidates through the use of the accelerated approval pathway or similar expedited approval pathways outside the US. 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 or similar expedited approval by foreign regulatory authorities, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA or foreign regulatory authorities may seek to withdraw accelerated approval or similar conditional approval.

We are developing certain product candidates for the treatment of serious and life-threatening conditions, and therefore may decide to seek approval of such product candidates under the FDA's accelerated approval pathway. A product candidate may be eligible for accelerated approval if it is designed to treat a serious or life-threatening disease or condition and generally provides a meaningful advantage 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, confirmatory studies to verify and describe the drug's clinical benefit. If the sponsor fails to conduct such studies in a timely manner, or if such confirmatory studies fail to verify the drug's predicted clinical benefit, the FDA may withdraw its approval of the drug on an expedited basis. In addition, in December 2022, the President signed an omnibus appropriations bill to fund the US government through fiscal year 2023. Included in the omnibus bill is the Food and Drug Omnibus Reform Act of 2022, which among other things, introduced reforms intended to expand the FDA's ability to regulate products receiving accelerated approval, including by increasing the FDA's oversight over the conduct of confirmatory trials; however, the ultimate impact of these reforms remains unclear.

In the EU, a "conditional" marketing authorization may be granted in cases where all the required safety and efficacy data are not yet available. A conditional marketing authorization is subject to conditions to be fulfilled for generating missing data or ensuring increased safety measures. A conditional marketing authorization is valid for one year and has to be renewed annually until fulfillment of all relevant conditions. Once the applicable pending studies are provided, a conditional marketing authorization can become a "standard" marketing authorization. However, if the conditions are not fulfilled within the timeframe set by the European Medicines Agency ("EMA"), the marketing authorization will cease to be renewed. Furthermore, marketing authorizations 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 the introduction of specific procedures. This may arise 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 type of marketing authorization is close to a 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 a marketing authorization. However, unlike a conditional marketing authorization, the applicant does not have to provide the missing data and will never have to. Although a marketing authorization "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the marketing authorization may be withdrawn where the risk-benefit ratio is no longer favorable.

The competent regulatory authorities in the EU have broad discretion whether to grant such a conditional marketing authorization or marketing authorization under exceptional circumstances, and, even if such assessment or authorization is granted, we may not experience a faster development process, review or authorization compared to conventional procedures. Moreover, the removal or threat of removal of such marketing authorizations may create uncertainty or delay in the clinical development of our product candidates and threaten the commercialization prospects of our products and product candidates, if approved. Such an occurrence could materially impact our business, financial condition and results of operations.

If we decide to submit an NDA seeking accelerated approval or receive an expedited regulatory designation for our product candidates, 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. Failure to obtain accelerated approval or any other form of expedited development, review or approval for a product candidate would result in a longer time period prior to commercialization of such product candidate, if any, and could increase the cost of development of such product candidate, which could harm our competitive position in the marketplace.

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us or any future collaboration partners from obtaining approvals for the commercialization of any product candidate we develop.

Any product candidates we may develop and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities in the US and by comparable authorities in other countries. Any product candidates we develop may not be effective, may be only moderately effective, or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate in a given jurisdiction. We have not received approval to market any product candidates from regulatory authorities in any jurisdiction. It is possible that none of the product candidates we are developing or that we may seek to develop in the future will ever obtain regulatory approval. We, as a company, have no experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party CROs, suppliers, vendors or regulatory consultants to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority.

The process of obtaining marketing approvals, both in the US and abroad, is expensive, may take many years if numerous clinical trials are required, 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. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application**.** 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. A proposal for revision of several legislative instruments related to medicinal products (potentially revising the duration of regulatory exclusivity, eligibility for expedited pathways, etc.) is expected to be adopted by the European Commission during the first quarter of 2023. The proposed revisions, once they are agreed and adopted by the European Parliament and European Council (not expected before the end of 2024 or early 2025) may have a significant impact on the pharmaceutical industry in the long term.

The FDA and comparable authorities in other countries 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 ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of any product candidates we may develop, the commercial prospects for those product candidates may be harmed, and our ability to generate product revenue will be materially impaired.

We may seek an EUA from the FDA or comparable emergency use authorizations from foreign regulatory authorities with respect to our bemnifosbuvir COV19 product candidates in development for the treatment of COVID-19, and if we fail to obtain or maintain such authorizations, we may be required to pursue a more lengthy clinical development process than we expect, and our business may be harmed.

If available at the time we have sufficient data from our Phase 3 SUNRISE-3 clinical trial and other COVID-19 clinical trials, we may seek an EUA from the FDA or comparable emergency use authorizations from other foreign regulatory authorities with respect to our bemnifosbuvir COV19 product candidates. The FDA has the authority to issue an EUA only under certain circumstances, such as during

a public health emergency, pursuant to a declaration by the Secretary of the Department of Health and Human Services, or HHS, that an emergency exists justifying the issuance of EUAs for certain types of products (referred to as EUA declarations). On March 27, 2020, the Secretary of HHS declared that circumstances then existed that justified authorization of drugs and biologics during the COVID-19 pandemic, subject to the terms of any EUA that subsequently issued for a specific product. Once an EUA declaration has been issued and remains in place, the FDA can issue EUAs for products that fall within the scope of that declaration. To issue an EUA, the FDA Commissioner must conclude that (1) the chemical, biological, radioactive or nuclear agent, or CBRN, that is referred to in the EUA declaration can cause serious or life-threatening diseases or conditions; (2) based on the totality of scientific evidence available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing the disease or condition attributable to the CBRN and that the product's known and potential benefits outweigh its known and potential risks; and (3) there is no adequate, approved, and available alternative to the product. Currently there are two oral direct acting antivirals Paxlovid™(nirmatrelvir and ritonavir) and LAGEVRIO® (molnupiravir) authorized for emergency use for high risk COVID-19 patients.

The FDA's standards for granting an EUA are lower than for approving NDAs in accordance with traditional review procedures, and even if we seek and obtain an EUA for one or more of our product candidates, we cannot assure you that the FDA would approve a NDA for such product candidate, if such approval is required. Accordingly, even if we obtain an EUA for a bemnifosbuvir COV19 product candidate, we may be required to conduct additional clinical trials before we are able to submit an NDA or comparable marketing applications for such product candidate.

The authorization to market products under an EUA is limited to the period of time the EUA declaration is in effect, and the FDA can revoke an EUA in certain circumstances. The FDA's policies regarding an EUA can change unexpectedly. We cannot predict how long any authorization, if obtained, will remain in place. The FDA's policies regarding vaccines and other products used to diagnose, treat or mitigate COVID-19 remain in flux as the FDA responds to new and evolving public health information and clinical evidence. On January 31, 2023, the Biden Administration announced its plan to terminate the public health emergency, or PHE, for COVID-19 effective as of May 11, 2023. In the absence of a declaration of a PHE, the Secretary of HHS may determine that the circumstances justifying the issuance of future EUAs have also lapsed. In such case, we would be required to seek an NDA in order to commercialize any bemnifosbuvir COV19 product candidate.

Therefore, even if we believe the data from our Phase 3 SUNRISE-3 clinical trial and any other COVID-19 clinical trials we may initiate are positive, we may be unable to obtain an EUA or other emergency authorizations for a bemnifosbuvir COV19 product candidate. Moreover, even if we do obtain an EUA or comparable emergency authorization, it is possible that such EUA or other authorizations may be revoked and we may be required to cease any commercialization activities, until, if ever, we receive NDA approval for such product. Any cessation of commercialization activities would adversely impact our business, financial condition and results of operations.

Even if we obtain FDA approval of any of our product candidates, we may never obtain approval or commercialize such products outside of the US, which would limit our ability to realize their full market potential.

In order to market any products outside of the US, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials which would be costly and time-consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time-consuming, uncertain and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and as an organization we do not have experience in

obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our ability to realize the full market potential of our products will be harmed.

Even if a current or future product candidate receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any current or future product candidate we develop receives marketing approval, whether as a single agent or in combination with other therapies, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, current approved antiviral products are well established in the medical community for the treatment of HCV and in the US, two oral antivirals, Paxlovid and Lagevrio, are currently authorized for the treatment of COVID-19, and doctors may continue to rely on these therapies. If the product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of any product candidate, if approved for commercial sale, will depend on a number of factors, including but not limited to:

- efficacy and potential advantages compared to alternative treatments;
- the ability to offer our products, if approved, for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the ability to obtain sufficient third-party coverage and adequate reimbursement, including with respect to the use of the approved product as a combination therapy;
- adoption of a companion diagnostic and/or complementary diagnostic; and
- the prevalence and severity of any side effects.

Disruptions at the FDA and foreign regulatory authorities caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA and foreign regulatory authorities to review or approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's or foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's or foreign regulatory authorities' ability to perform routine functions including a rapid substantial influx of applications from numerous sponsors as occurred with COVID-19. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government agencies 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 drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the US government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, the FDA postponed most inspections of domestic and foreign manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations of domestic facilities where feasible, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID-19 pandemic, and any resurgence of the virus or emergence of new variants may lead to further inspectional delays. Regulatory authorities outside the US have adopted similar restrictions or other policy measures in response to the COVID-19 pandemic. If a

prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Our insurance policies are expensive and protect us only from some business risks, which leaves us exposed to significant uninsured liabilities.

Though we have insurance coverage for clinical trial product liability, we do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, property, auto, workers' compensation, umbrella, and directors' and officers' insurance.

As a part of the clinical trial regulatory submission process, in many countries, we are required to provide local insurance coverage covering claims that persons associated with the clinical trial may assert if they are or believe they are injured as a result of participation in the clinical trial or contact with the investigational product candidate being studied in the clinical trial. These local insurance policies can be time consuming to obtain which may delay the anticipated start of a clinical trial in a particular country. Additionally, these local insurance policies may not cover all the claims an injured party may assert and may be insufficient to cover the losses associated with our defense of the claim and any judgement against us that may result.

Any additional product liability insurance coverage we acquire in the future may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If we obtain marketing approval for any of our product candidates, we intend to acquire insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments are for claims not covered by or are in amounts that exceed our insurance coverage, could adversely affect our results of operations and business, including preventing or limiting the development and commercialization of any product candidates we develop. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

Operating as a public company has and may in the future make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our board of directors, our board committees or as executive officers. We do not know, however, if we will be able to maintain existing insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our cash and cash equivalents position and results of operations.

Our business and operations may suffer in the event of information technology system failures, cyberattacks, or deficiencies, which could materially affect our results.

Our information technology systems, as well as those of our CROs and other contractors and consultants, are vulnerable to attack, failure and damage from computer viruses and other malware (e.g., ransomware), unauthorized access or other cybersecurity attacks, malfeasance by external or internal parties, human error (e.g., social engineering, phishing), natural disasters (including hurricanes), terrorism, war, fire and telecommunication or electrical failures. In the ordinary course of our business, we directly or indirectly collect, store and transmit sensitive data, including intellectual property, confidential information, preclinical and clinical trial data, proprietary business information, personal data and personally identifiable health information of our clinical trial subjects and employees, in our data centers and on our networks, or on those of third parties. The secure processing, maintenance and transmission of this information is critical to our operations.

Despite security measures that we and our critical third parties (e.g., collaborators) implement, our information technology systems may be vulnerable to attacks by hackers or internal bad actors, or breached due to human error, a technical vulnerability, malfeasance or other disruptions. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, level of persistence, intensity and sophistication of attempted attacks and intrusions from around the world have increased. As a result of the COVID-19 pandemic, we also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. We may not be able to anticipate all types of security threats, nor may we be able to implement preventive measures effective against all such security threats. The techniques used by cybercriminals 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. Because of this, we may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attacks increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. We cannot assure you that our data protection efforts and our investment in information technology will prevent significant breakdowns, data leakages or breaches in our systems or those of our CROs and other contractors and consultants.

We and certain of our service providers are from time to time subject to cyberattacks and security incidents. While we do not believe that we have experienced any significant system failure, accident 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 product candidate development programs. For example, the loss data from completed, ongoing or planned preclinical studies or clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of personal, confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

If a security breach or other incident were to result in the unauthorized access to or unauthorized use, disclosure, release or other processing of personal information, it may be necessary to notify individuals, governmental authorities, supervisory bodies, the media and other parties pursuant to privacy and security laws. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information and significant regulatory penalties, and such an event could disrupt our operations, damage our reputation and cause a loss of confidence in us and our ability to conduct clinical trials, which could adversely affect our reputation and delay our clinical development of our product candidates. Further, our insurance coverage may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems.

Risks Related to Healthcare Laws and Other Legal Compliance Matters

We will be subject to extensive and costly government regulation.

Our product candidates will be subject to extensive and rigorous domestic government regulation, including regulation and oversight by the FDA, the Centers for Medicare & Medicaid Services (“CMS”), other divisions of the US Department of Health and Human Services, the US Department of Justice, state and local governments, and their respective equivalents outside of the US. The FDA regulates the research, development, preclinical and clinical testing, manufacture, safety, effectiveness, record-keeping, reporting, labeling, packaging, storage, approval, advertising, promotion, sale, distribution, import and export of pharmaceutical products. If our products are marketed abroad, they will also be subject to extensive regulation by foreign governments, whether or not they have obtained FDA approval. Such foreign regulation may be equally or more demanding than corresponding US regulation.

Government regulation substantially increases the cost and risk of researching, developing, manufacturing and selling our products. The regulatory review and approval process, which includes preclinical testing and clinical trials of each product candidate, is lengthy, expensive and uncertain. We

must obtain and maintain regulatory authorization to conduct clinical trials. We must obtain regulatory approval for each product we intend to market, and the manufacturing facilities used for the products must be inspected and meet legal requirements. Securing regulatory approval requires the submission of extensive preclinical and clinical data and other supporting information for each proposed therapeutic indication in order to establish the product's safety and efficacy, potency and purity, for each intended use. The development and approval process takes many years, requires substantial resources, and may never lead to the approval of a product.

Even if we are able to obtain regulatory approval for a particular product, the approval may limit the indicated medical uses for the product, may otherwise limit our ability to promote, sell and distribute the product, may require that we conduct costly post-marketing surveillance, and/or may require that we conduct ongoing post-marketing studies. Material changes to an approved product, such as, for example, manufacturing changes or revised labeling, may require further regulatory review and approval. Once obtained, any approvals may be withdrawn, including, for example, if there is a later discovery of previously unknown problems with the product, such as a previously unknown safety issue.

If we, our consultants, CMOs, CROs or other vendors, fail to comply with applicable regulatory requirements at any stage during the regulatory process, such noncompliance could result in, among other things, delays in the approval of applications or supplements to approved applications; refusal of a regulatory authority, including the FDA, to review pending market approval applications or supplements to approved applications; warning letters; fines; import and/or export restrictions; product recalls or seizures; injunctions; total or partial suspension of production; civil penalties; withdrawals of previously approved marketing applications or licenses; recommendations by the FDA or other regulatory authorities against governmental contracts; and/or criminal prosecutions.

Enacted and future healthcare legislation and policies may increase the difficulty and cost for us to commercialize our product candidates and could adversely affect our business.

In the US, the EU and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities involving any product candidates for which we obtain marketing approval, impact pricing and reimbursement and impact our ability to sell any such products profitably. In particular, there have been and continue to be a number of initiatives at the US federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. In addition, new regulations and interpretations of existing healthcare statutes and regulations are frequently adopted.

In March 2010, the Patient Protection and Affordable Care Act ("ACA"), was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs;
- a new Medicare Part D coverage gap discount program, requiring manufacturers to agree to offer point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- increases and changes in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- extension of a manufacturer's Medicaid rebate liability to covered outpatient drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of the Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial, Congressional and executive challenges to certain aspects of the ACA On June 17, 2021, the US Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA.

In addition, other legislative changes have been proposed and adopted in the US since the ACA was enacted. In August 2011, the Budget Control Act of 2011 imposed aggregate reductions of Medicare payments to providers, effective April 1, 2013 which, due to subsequent legislative amendments, will stay in effect through 2031. Further, on March 11, 2021 the American Rescue Plan Act of 2021 was signed into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, beginning January 1, 2024.

Moreover, payment methodologies may be subject to other changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as outcomes-based reimbursement. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several US Congressional inquiries and proposed and enacted federal legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs. Most recently, on August 16, 2022, the Inflation Reduction Act ("IRA") was signed into law. 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 Department of Health and Human Services ("HHS") to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated. We expect that additional US federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the US federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Individual states in the US have also increasingly passed legislation and implemented 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. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing.

In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of

healthcare and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved.

In markets outside of the US and the EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

Enacted and future legislation and policies may increase the difficulty and cost for us to obtain marketing approval of our product candidates and could adversely affect our business.

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

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the US, the EU or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, we may be subject to enforcement action and we may not achieve or sustain profitability.

Even if we obtain regulatory approval for a product candidate, our products will remain subject to regulatory scrutiny and post-marketing requirements.

Any regulatory approvals that we may receive for our product candidates will require the submission of reports to regulatory authorities and surveillance to monitor the safety and efficacy of the product candidate, may contain significant limitations related to use restrictions for groups specified by, among other things, age or medical condition, warnings, precautions or contraindications, and may include burdensome post-approval study or risk management requirements. For example, the FDA may require a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if one of our product candidates is approved, it will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies and submission of safety, efficacy, and other post- market information, including both federal and state requirements in the US and requirements of comparable foreign regulatory authorities. Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP and similar regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and similar requirements and adherence to commitments made in any approved marketing application. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

If the FDA or another regulatory authority discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, such regulatory authorities may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory authority or enforcement authority may, among other things:

- issue warning letters;

- impose civil or criminal penalties;
- suspend or withdraw regulatory approval;
- suspend any of our clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities; or
- seize or detain products, or require a product recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, our business will be seriously harmed.

Moreover, the policies of the FDA and of other regulatory authorities may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the US or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action, and we may not achieve or sustain profitability.

The FDA and other regulatory agencies 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 and other regulatory agencies 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 for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The US 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.

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, and if approved, market, sell and distribute our product candidates,. Such laws include but are not limited to:

- the US federal Anti-Kickback Statute, which makes it illegal for any person to knowingly and willfully solicit, offer, receive, pay or provide any remuneration (including any kickback, bribe or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or

recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under US federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the US federal civil and criminal false claims laws, including the civil False Claims Act ("FCA"), which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the US federal government, claims for payment or approval that are false, fictitious or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the US federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The government may deem manufacturers to have "caused" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. Companies that submit claims directly to payors may also be liable under the FCA for the direct submission of such claims. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the FCA, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;
- the federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer of remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner or supplier of services reimbursable by Medicare or a state healthcare program, unless an exception applies;
- the US federal Health Insurance Portability and Accountability Act of 1996, ("HIPAA") and its implementing regulations, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the US federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- the US Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the government information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants and certified nurse midwives), and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;

- federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where reported prices may be used in the calculation of reimbursement and/or discounts on approved products;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- analogous US state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the US federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and state and local laws that require the registration of pharmaceutical sales representatives; and
- similar healthcare laws and regulations in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices, including our relationships with physicians and other healthcare providers, some of whom are compensated in the form of stock or stock options for services provided to us and may be in the position to influence the ordering of or use of our product candidates, if approved, may not comply with current or future statutes, regulations, agency guidance 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 the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time-consuming and may require significant 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.

We are subject to governmental regulation and other legal obligations, particularly related to privacy, data protection and information security, and we are subject to consumer protection laws that regulate our marketing practices and prohibit unfair or deceptive acts or practices. Our actual or perceived failure to comply with such obligations could harm our business.

We are subject to diverse laws and regulations relating to data privacy and security. New privacy rules are being enacted in the US and globally, and existing ones are being updated and strengthened. For example, the California Consumer Privacy Act ("CCPA") went into effect on January 1, 2020 and creates individual privacy rights for California consumers, increases the privacy and security obligations of entities handling certain personal information, requires new disclosures to California individuals and affording such individuals new abilities to opt out of certain sales of personal information, and provides for civil penalties for violations as well as a private right of action for data breaches that is expected to increase data breach litigation. Further, the California Privacy Rights Act ("CPRA"), which generally went into effect on January 1, 2023, significantly amends the CCPA and imposes additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It has also created a new

California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement, and additional compliance investment and potential business process changes may be required. Similar laws have passed in Virginia, Colorado, Connecticut and Utah, and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the US. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

Complying with these numerous, complex and often changing regulations is expensive and difficult, and failure to comply with any privacy laws or data security laws or any security incident or breach involving the misappropriation, loss or other unauthorized processing, use or disclosure of sensitive or confidential patient, consumer or other personal information, whether by us, one of our CROs or business associates or another third-party, could adversely affect our business, financial condition and results of operations. Such adverse effects may include, but are not limited to: investigation costs; material fines and penalties; compensatory, special, punitive and statutory damages; litigation; consent orders regarding our privacy and security practices; requirements that we provide notices, credit monitoring services and/or credit restoration services or other relevant services to impacted individuals; adverse actions against our licenses to do business; reputational damage; and injunctive relief.

Our operations abroad may also be subject to increased scrutiny or attention from data protection authorities. For example, the EU GDPR went into effect in May 2018, and imposes strict requirements for processing the personal data of individuals within the EEA or in the context of our activities in the EEA. The GDPR and related implementing laws in individual EU member states govern the collection and use of health data and other personal data in the EU including the personal data processed by companies outside the EU in connection with the offering of goods or services to individuals in the EU or the monitoring of their behavior (including in the context of clinical trials). Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. In addition to the foregoing, a breach of the GDPR could result in regulatory investigations, reputational damage, orders to cease / change our processing of our data, enforcement notices, and/ or assessment notices (for a compulsory audit). Companies may also face civil claims including representative actions and other class action type litigation (where individuals have suffered harm), potentially amounting to significant compensation or damages liabilities, as well as associated costs, diversion of internal resources, and reputational harm.

Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the US; in July 2020 the Court of Justice of the EU ("CJEU") limited how organizations could lawfully transfer personal data from the EEA to the US by invalidating the Privacy Shield for purposes of international transfers and imposing further restrictions on use of the standard contractual clauses ("SCCs"). In March 2022, the US and EU announced a new regulatory regime intended to replace the invalidated regulations; however, this new EU-US Data Privacy Framework has not been implemented beyond an executive order signed by President Biden on October 7, 2022 on Enhancing Safeguards for US Signals Intelligence Activities. European court and regulatory decisions subsequent to the CJEU decision of July 16, 2020 have taken a restrictive approach to international data transfers. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the SCCs cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.

In addition, from January 1, 2021, after the end of the transition period following the UK's departure from the EU, we are also subject to the UK data protection regime (the UK GDPR and UK Data Protection Act 2018), which imposes separate but similar obligations to those under the GDPR and comparable penalties, including fines of up to £17.5 million or 4% of a noncompliant company's global annual revenue for the preceding financial year, whichever is greater.

We cannot assure you that our CROs or other third-party service providers with access to our or our suppliers', trial patients', investigators and clinical site employees' personally identifiable and other sensitive or confidential information in relation to which we are responsible will not breach contractual obligations imposed by us, or that they will not experience data security breaches or attempts thereof, which could have a corresponding effect on our business, including putting us in breach of our obligations under privacy laws and regulations and/or which could in turn adversely affect our business, results of operations and financial condition. We cannot assure you that our contractual measures and our own privacy and security-related safeguards will protect us from the risks associated with the third-party processing, use, storage and transmission of such information. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We face potential liability related to the privacy of health information we obtain from clinical trials sponsored by us.

Most healthcare providers in the US, including research institutions from which we obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act. We do not believe that we are currently acting as a covered entity or business associate under HIPAA and thus are not directly subject to its requirements or penalties. However, any person may be prosecuted under HIPAA's criminal provisions either directly or under aiding-and-abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has not satisfied HIPAA's requirements for disclosure of individually identifiable health information. Even when HIPAA does not apply, according to the Federal Trade Commission ("FTC"), failing to take appropriate steps to keep consumers' personal information secure constitutes unfair acts or practices in or affecting commerce in violation of the Federal Trade Commission Act. The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards.

We, our CROs and third-party service providers receive and maintain sensitive information, including health-related information, that we receive throughout the clinical trial process, in the course of our research collaborations. As such, we may be subject to state laws, requiring notification of affected individuals and state regulators in the event of a breach of personal information, which is a broader class of information than the health information protected by HIPAA. Our clinical trial programs outside the US may implicate international data protection laws, including the UK GDPR, GDPR and legislation of the EU member states implementing it. In addition, the EU adopted the EU Clinical Trials regulation, which came into effect on January 31, 2022. This regulation imposes new obligations on the use of data generated from clinical trials and enables European patients to have the opportunity to access their personal data processed in the context of clinical trials.

Our activities outside the US impose additional compliance requirements and generate additional risks of enforcement for noncompliance. Failure by our CROs and other third-party contractors to comply with the strict rules on the transfer of personal data outside of the EU into the US may result in the imposition of criminal and administrative sanctions on such collaborators, which could adversely affect our business. Furthermore, certain health privacy laws, data breach notification laws, consumer protection laws and genetic testing laws may apply directly to our operations and/or those of our collaborators and may impose restrictions on our collection, use and dissemination of individuals' health information.

Moreover, patients about whom we or our collaborators obtain health information, as well as the providers who share this information with us, may have statutory or contractual rights that limit our ability to use and disclose the information. We may be required to expend significant capital and other resources to ensure ongoing compliance with applicable privacy and data security laws. Claims that we have violated individuals' privacy rights or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

If we or third-party CMOs, CROs or other contractors or consultants fail to comply with applicable federal, state or foreign regulatory privacy requirements, we could be subject to a range of regulatory actions that could affect our or our contractors' ability to develop and commercialize our product candidates and could harm or prevent sales of any affected products that we are able to commercialize, or could substantially increase the costs and expenses of developing, commercializing and marketing our products. Any threatened or actual government enforcement action could also generate adverse publicity and require that we devote substantial resources that could otherwise be used in other aspects of our business. Increasing use of social media could give rise to liability, breaches of data security or reputational damage. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

We are subject to environmental, health and safety laws and regulations, and we may become exposed to liability and substantial expenses in connection with environmental compliance or remediation activities.

Our operations, including our development, testing and manufacturing activities, are subject to numerous environmental, health and safety laws and regulations. These laws and regulations govern, among other things, the controlled use, handling, release and disposal of and the maintenance of a registry for, hazardous materials and biological materials, such as chemical solvents, human cells, carcinogenic compounds, mutagenic compounds and compounds that have a toxic effect on reproduction, laboratory procedures and exposure to blood-borne pathogens. If we fail to comply with such laws and regulations, we could be subject to fines or other sanctions. Moreover, certain environmental laws may impose liability without regard to fault or legality of the action at the time of its occurrence.

As with other companies engaged in activities similar to ours, we face a risk of environmental liability inherent in our current and historical activities, including liability relating to releases of or exposure to hazardous or biological materials. Environmental, health and safety laws and regulations are becoming more stringent. We may be required to incur substantial expenses in connection with future environmental compliance or remediation activities, in which case, the production efforts of our third-party manufacturers or our development efforts may be interrupted or delayed.

We and our employees are increasingly utilizing social media tools as a means of communication both internally and externally.

Despite our efforts to monitor evolving social media communication guidelines and comply with applicable rules, there is risk that the use of social media by us or our employees to communicate about our product candidates or business may cause us to be found in violation of applicable requirements. In addition, our employees may knowingly or inadvertently make use of social media in ways that may not comply with applicable laws and regulations, our policies and other legal or contractual requirements, which may give rise to regulatory enforcement action, liability, lead to the loss of trade secrets or other intellectual property or result in public exposure of personal information of our employees, clinical trial patients, customers and others. Furthermore, negative posts or comments about us or our product candidates in social media could seriously damage our reputation, brand image and goodwill. Any of these events could have a material adverse effect on our business, prospects, operating results and financial condition and could adversely affect the price of our common stock.

Risks Related to Commercialization

Developments by competitors may render our products or technologies obsolete or non-competitive or may reduce the size of our markets.

Our industry has been characterized by extensive research and development efforts, rapid developments in technologies, intense competition and a strong emphasis on proprietary products. We expect our product candidates to face intense and increasing competition as new products enter the relevant markets and advanced technologies become available. We face potential competition from many different sources, including pharmaceutical, biotechnology and specialty pharmaceutical companies. Academic research institutions, governmental agencies and public and private institutions are also potential sources of competitive products and technologies. Our competitors may have or may develop superior technologies or approaches, which may provide them with competitive advantages. Many of these competitors may also have products already approved or in development in the therapeutic categories

that we are targeting with our product candidates. In addition, many of these competitors, either alone or together with their collaborative partners, may operate larger research and development programs or have substantially greater financial resources than we do, as well as greater experience in:

- developing product candidates;
- undertaking preclinical testing and clinical trials;
- obtaining NDA approval by the FDA and comparable approvals of product candidates from foreign regulatory authorities;
- formulating and manufacturing products; and
- launching, marketing and selling products.

If these competitors access the marketplace before we do with safer, more effective, or less expensive therapeutics or vaccines, our product candidates, if approved for commercialization, may not be profitable to sell or worthwhile to continue to develop. Technology in the pharmaceutical industry has undergone rapid and significant change, and we expect that it will continue to do so. Any compounds, products or processes that we develop may become obsolete or uneconomical before we recover any expenses incurred in connection with their development. The success of our product candidates will depend upon factors such as product efficacy, safety, reliability, availability, timing, scope of regulatory approval, acceptance and price, among other things. Other important factors to our success include speed in developing product candidates, completing clinical development and laboratory testing, obtaining regulatory approvals and manufacturing and selling commercial quantities of potential products.

Significant competition exists from approved treatments and, in the case of COVID-19, authorized treatments or treatments in development for the diseases that we are targeting. Many of the approved drugs are well-established therapies or products and are widely accepted by physicians, patients and third-party payors. There are pharmaceutical and biotechnology companies at various stages of development and approval of vaccines and therapeutics for COVID-19 and treatments for each of the disease indications we are targeting. Currently there are several vaccines and associated vaccine boosters approved or authorized for use for COVID-19 and there are therapeutics available for the treatment of COVID-19 including two oral antiviral therapies, Paxlovid™ and Lagevrio™ each of which are authorized for emergency use for high risk COVID-19 patients. Additionally, Veklury, a nucleotide prodrug, which is intravenously administered is approved for the treatment of COVID-19 in adults and pediatric patients who are hospitalized or if not hospitalized have mild to moderate COVID-19 and are at high risk for progression to severe COVID-19, including hospitalization and death. Treatments in development for COVID-19 include GS-5245, an oral nucleoside prodrug, that is being evaluated by Gilead Sciences in a randomized, double-blind placebo controlled trial in non-hospitalized COVID patients who are at high risk of progression to hospitalization. There are also several drugs, including oral antivirals such as Epclusa® and Mavyret®, approved for the treatment of HCV Our product candidates are intended to compete directly or indirectly with existing products and products currently in development. Even if approved and commercialized, our product candidates may fail to achieve market acceptance with hospitals, physicians or patients. Hospitals, physicians or patients may conclude that our products are less safe or effective or otherwise less attractive than existing drugs. If our product candidates do not receive market acceptance for any reason, our revenue potential would be diminished, which would materially adversely affect our ability to become profitable.

Many of our competitors have substantially greater capital resources, robust product candidate pipelines, established presence in the market and expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing approved products than we do. As a result, our competitors may achieve product commercialization or patent or other intellectual property protection earlier than we can. 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 clinical, regulatory, scientific, sales, marketing 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, our programs. 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 may develop or that would render any products that we may develop obsolete or noncompetitive, which would have a material adverse effect on our business and operations.

The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate product revenue.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the US, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs and biologics when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing third-party therapeutics may limit the amount we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates and may not be able to obtain a satisfactory financial return on our product candidates.

In the US, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered and reimbursed. The Medicare program is increasingly used as a model for how private and other governmental payors develop their coverage and reimbursement policies for new drugs. However, no uniform policy for coverage and reimbursement for products exists among third-party payors in the US. Therefore, 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 product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Some third-party payors may require pre-approval of coverage for new or innovative drug therapies before they will reimburse healthcare providers who use such therapies. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely. We cannot predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

Outside the US, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in the EU and other jurisdictions have and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other

changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the US, the reimbursement for our product candidates may be reduced compared with the US and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the US and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes resulting from legislative actions, including the recently enacted IRA. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products.

In addition, since the Secretary of HHS in March 2020 declared a public health emergency at the outset of the COVID-19 pandemic, the US federal government has been a primary purchaser of therapeutics for the treatment of COVID-19. On January 31, 2023, the Biden Administration announced its plan to terminate the PHE for COVID-19, effective as of May 11, 2023. Even if we succeed in developing a bemnifosbuvir COV19 product candidate, we may not be able to compete effectively if such product does not satisfy government procurement requirements and our future results of operations may be adversely impacted if government procurement needs for such products decline due to over-saturated supply, reduced patient demand or reduced appropriations for such purchases. Additionally, it is uncertain for how long the US federal government will remain a primary purchaser of COVID-19 therapeutics. Recently, there have been announcements regarding the intention of the US federal government to transition the procurement and distribution of COVID-19 therapeutics, vaccines and diagnostic tests to the commercial market. The time at which this transition will occur is uncertain and is subject to many conditions including among others whether substantial incremental appropriations will be available to further fund the US federal government COVID-19 response. The effects of such a transition from US federal government procurement and distribution to commercial market channels are many and will likely include discontinuation of free or heavily subsidized access by US persons to COVID-19 therapeutics, vaccines and diagnostics. Such changes in patient access may affect product utilization and could limit our ability to successfully commercialize our product candidates and obtain a satisfactory financial return on our product candidates in this therapeutic space.

If we are unable to establish sales, marketing and distribution capabilities either on our own or in collaboration with third parties, we may not be successful in commercializing any of our product candidates, if approved, and we may not be able to generate any product revenue.

We have limited personnel or infrastructure for the sales, marketing or distribution of products, and no experience as a company in commercializing a product candidate. The cost of building and maintaining such an organization may exceed the cost-effectiveness of doing so.

We may build our own focused sales, distribution and marketing infrastructure to market our product candidates, if approved, in the US and other markets around the world. There are significant expenses and risks involved with building our own sales, marketing and distribution capabilities, including our ability to hire, retain and appropriately incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities could delay any product launch, which would adversely impact the commercialization of our product candidate, if approved. Additionally, if the commercial launch of our product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own include but are not limited to:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe our future products;
- our inability to equip medical and sales personnel with effective materials, including medical and sales literature to help them educate physicians and other healthcare providers regarding applicable diseases and our future products;
- 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 product lines;
- our inability to develop or obtain sufficient operational functions to support our commercial activities; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable or decide not to establish internal sales, marketing and distribution capabilities, or decide not to do so for a particular country, we may pursue collaborative arrangements. If we pursue a collaborative arrangement, our sales will largely depend on the collaborator's strategic interest in the product and such collaborator's ability to successfully commercialize the product.

If we are unable to build our own sales force or access a collaborative relationship for the commercialization of any of our product candidates, we may be forced to delay the potential commercialization of our product candidates or reduce the scope of our sales or marketing activities for such product candidates. If we elect to increase our expenditures to fund commercialization activities ourselves, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. We could enter into arrangements with collaborative partners at an earlier stage than otherwise would be ideal and we may be required to relinquish rights to any of our product candidates or otherwise agree to terms unfavorable to us, any of which may have an adverse effect on our business, operating results and prospects.

If we are unable to establish adequate sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates and may not become profitable and may incur significant additional losses. We will be competing with many companies, including large pharmaceutical companies, that have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third-party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

In addition, even if we do establish adequate sales, marketing and distribution capabilities, the progress of general industry trends with respect to pricing models, supply chains and delivery mechanisms, among other things, could deviate from our expectations. If these or other industry trends change in a manner which we do not anticipate or for which we are not prepared, we may not be successful in commercializing our product candidates or become profitable.

Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future profitability may depend, in part, on our ability to commercialize our product candidates in foreign markets for which we may rely on collaboration with third parties. We do not currently have any collaborator for the commercialization of any of our product candidates in foreign markets. We are evaluating the opportunities for the development and commercialization of our product candidates in foreign markets. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the applicable regulatory authority in that foreign market, and we may never receive such regulatory approval for any of our product candidates. To obtain separate regulatory approvals in other countries, we may be required to comply with numerous and varying regulatory requirements of such countries regarding the safety and efficacy of our product candidates and

governing, among other things, clinical trials and commercial sales, pricing and distribution of our product candidates, and we cannot predict success in these jurisdictions. If we obtain approval of our product candidates and ultimately commercialize our product candidates in foreign markets, we would be subject to additional risks and uncertainties, including but not limited to:

- our customers' ability to obtain reimbursement for our product candidates in foreign markets;
- our inability to directly control commercial activities if we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- our ability to supply our product candidates on a timely and large-scale basis in local markets;
- longer lead times for shipping which may necessitate local manufacture of our product candidates;
- language barriers for technical training and the need for language translations;
- reduced protection of patent and other intellectual property rights in some foreign countries;
- the existence of additional potentially relevant third-party intellectual property rights;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of any product for which we obtain approval could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

If any of our product candidates is approved for commercialization, we may selectively partner with third parties to market it in certain jurisdictions outside the US. We expect that we will be subject to additional risks related to international pharmaceutical operations, including but not limited to:

- different regulatory requirements for drug approvals and rules governing drug commercialization in foreign countries;
- reduced protection for patent and other intellectual property rights;
- foreign reimbursement, pricing and insurance regimes;
- potential noncompliance with the US Foreign Corrupt Practices Act, the U.K. Bribery Act 2010 and similar anti-bribery and anticorruption laws in other jurisdictions; and
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad.

As an organization, we have no prior experience in these areas. In addition, we will need to comply with complex regulatory, tax, labor and other legal requirements imposed by both the EU and many of the individual member states in the EU as well as in other global territories such as South America and Southeast Asia. Many US-based biotechnology companies have found the process of marketing products outside of North America to be very challenging.

Certain legal and political risks are also inherent in foreign operations. There is a risk that foreign governments may nationalize private enterprises in certain countries where we may operate. In certain countries or regions, terrorist activities and the response to such activities may threaten our operations

more than in the US. Social and cultural norms in certain countries may not support compliance with our corporate policies, including those that require compliance with substantive laws and regulations. Also, changes in general economic and political conditions in countries where we may operate are a risk to our financial performance and future growth. Additionally, the need to identify financially and commercially strong partners for commercialization outside the US who will comply with the high manufacturing and legal and regulatory compliance standards we require is a risk to our financial performance. As we operate our business globally, our success will depend, in part, on our ability to anticipate and effectively manage these and other related risks. There can be no assurance that the consequences of these and other factors relating to our international operations will not have an adverse effect on our business, financial condition or results of operations.

In some countries, particularly in the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we may be required to conduct clinical trials that compare the cost-effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

Potential product liability lawsuits against us could cause us to incur substantial liabilities and limit commercialization of any products that we may develop.

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. On occasion, large judgments have been awarded in class action lawsuits based on products that had unanticipated adverse effects. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs, which may not be covered by insurance. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation and significant negative media attention;
- withdrawal of participants from our clinical trials;
- injury to our reputation;
- initiation of investigations by regulators;
- significant costs to defend the claims and related litigation;
- distraction of management’s attention from our primary business;
- substantial monetary awards to patients or other claimants;
- inability to commercialize a product candidate;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- exhaustion of any available insurance and our capital resources;
- decreased demand for a product candidate, if approved for commercial sale; and
- loss of revenue.

Failure to obtain or retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with corporate collaborators. Although we have clinical trial insurance, our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate

collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

Risks Related to Manufacturing and our Dependence on Third Parties

We rely and expect to continue to rely on third parties for the manufacture of materials for our research programs, preclinical studies and clinical trials and we do not have long-term contracts with any of these parties. This reliance on third parties increases the risk that we will not have sufficient quantities of such materials or any product candidates that we may develop and, if approved, commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.

We rely and expect to continue to rely on third parties for the manufacture of materials for our clinical trials and our research activities, preclinical and clinical development. We expect to rely on third parties for commercial manufacture if any of our product candidates receive marketing approval. We do not currently have a long-term agreement with any of the third-party manufacturers we currently use to provide preclinical and clinical trial materials, and we purchase any required materials on a purchase order basis. Certain of these manufacturers are critical to our production and the loss of these manufacturers, or an inability to obtain quantities at an acceptable cost or quality, could delay, prevent or impair our ability to timely conduct preclinical studies or clinical trials, and would materially and adversely affect our development and commercialization efforts.

We expect to rely on third-party manufacturers for the commercial supply of product candidates for which we obtain marketing approval, if any.

We may be unable to maintain or establish required agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including but not limited to:

- the failure of the third-party to manufacture our product candidates according to our schedule, or at all, including if our third-party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them as a result of accidents, fire, loss of personnel, business decisions at or by the third-party manufacturer or otherwise;
- the reduction or termination of production or deliveries by suppliers, or the raising of prices or renegotiation of terms;
- the termination or nonrenewal of arrangements or agreements by our third-party contractors at a time that is costly or inconvenient for us;
- the breach by the third-party contractors of our agreements with them;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the failure of the third-party to manufacture our product candidates according to our specifications;
- the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;
- improper handling of clinical supplies, whether during transit or otherwise, impacting the quality of such clinical supplies leading to loss of GMP status and the resulting inability to use such clinical supplies in clinical trials which may result in clinical interruptions and delays in the commencement of planned clinical trials;
- 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 misappropriation or unauthorized disclosure of our intellectual property or other proprietary information, including our trade secrets and know-how.

For ruzasvir, we have sole suppliers located in China for our active pharmaceutical ingredients, and for all our product candidates, including bemnifosbuvir, all suppliers of the regulatory starting materials for the respective manufacturing processes are located in China. We expect to continue to use such third-party manufacturers. Any disruption in production or inability of our manufacturers in China to produce adequate quantities to meet our needs, whether as a result of the current outbreak of COVID-19, a natural disaster, other pandemics, trade disruptions or other causes, could impair our ability to operate our business on a day-to-day basis and to continue our research and development of our product candidates. For example, the Uyghur Forced Labor Prevention Act bans imports from China's Xinjiang region unless it can be shown that the goods were not produced using forced labor and this legislation may have an adverse effect on global supply chains which could adversely impact our business and results of operations.

We do not have complete control over all aspects of the manufacturing process of, and are dependent on, our contract manufacturing partners for compliance with cGMP regulations and similar regulatory requirements for manufacturing both active drug substances and finished drug products. Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the US. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain authorization for their manufacturing facilities. In addition, we do not have control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not authorize these facilities for the manufacture of our product candidates or if it withdraws any such authorization in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market our product candidates, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates or drugs and harm our business and results of operations.

Our third-party manufacturers may be unable to successfully scale up manufacturing of our product candidates in sufficient quality and quantity, which may impair the clinical advancement and commercialization of our product candidates.

In order to conduct clinical trials of our product candidates and commercialize any approved product, our manufacturers need to manufacture them in large quantities. However, they may be unable to successfully increase the manufacturing capacity for any of our product candidates or products in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If we, or any manufacturers are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical trials of these product candidates may be delayed or infeasible, and regulatory approval or commercial launch of any resulting products may be delayed or not obtained, which could significantly harm our business. Supply sources could be interrupted from time to time and, if interrupted, would disrupt our manufacturers' ability to manufacture our product candidates at the scale required. If we are unable to meet the clinical or commercial supply need for our product candidates, or to do so on commercially reasonable terms, we may not be able to develop our product candidates and commercialize our products successfully.

We do not have multiple sources of supply for all of the components used in our product candidates, nor long-term supply contracts, and certain of our suppliers are critical to our production. If we were to lose a critical supplier, it could have a material adverse effect on our ability to complete the development of our product candidates. If we obtain regulatory approval for any of our product candidates, we would need to expand the supply of their components in order to commercialize them.

We do not have multiple sources of supply for all of the components used in the manufacture of bemnifosbuvir or ruzasvir or any of our other product candidates. For ruzasvir, we have sole suppliers located in China for our active pharmaceutical ingredients, and for all our product candidates, including bemnifosbuvir, all suppliers of the regulatory starting materials for the respective manufacturing

processes are located in China. We do not have long-term supply agreements with any of our component suppliers. We may not be able to establish additional sources of supply for our product candidates, or may be unable to do so on acceptable terms. Manufacturing suppliers are subject to cGMP quality and regulatory requirements and similar regulatory requirements, covering manufacturing, testing, quality control and record keeping relating to our product candidates and subject to ongoing inspections by applicable regulatory authorities. Manufacturing suppliers are also subject to local, state and federal regulations and licensing requirements. Failure by any of our suppliers to comply with all applicable regulations and requirements may result in long delays and interruptions in supply.

The number of suppliers of the components of our product candidates is limited. In the event it is necessary or desirable to acquire supplies from alternative suppliers, we might not be able to obtain them on commercially reasonable terms, if at all. It could also require significant time and expense to redesign our manufacturing processes to work with another company and redesign of processes can trigger the need for conducting additional studies such as comparability or bridging studies. Additionally, certain of our suppliers are critical to our production, and the loss of these suppliers to one of our competitors or otherwise would materially and adversely affect our development and commercialization efforts.

As part of any marketing approval, regulatory authorities conduct inspections that must be successful prior to the approval of the product. Failure of manufacturing suppliers to successfully complete these regulatory inspections will result in delays. If supply from the approved supplier is interrupted, there could be a significant disruption in commercial supply. An alternative vendor would need to be qualified through a NDA amendment or supplement, which could result in further delay. The FDA or other regulatory authorities outside of the US may also require additional studies if a new supplier is relied upon for commercial production. Switching vendors may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

If we are unable to obtain the supplies we need at a reasonable price or on a timely basis, it could have a material adverse effect on our ability to complete the development of our product candidates or, if we obtain regulatory approval for our product candidates, to commercialize them.

We rely on third parties to conduct our preclinical studies and clinical trials. Any failure by a third-party to conduct the clinical trials according to GCPs and in a timely manner may delay or prevent our ability to seek or obtain regulatory approval for or commercialize our product candidates.

We are dependent on third parties to conduct critical aspects of our Phase 3 SUNRISE-3 clinical trial, our preclinical studies and our other clinical trials and we expect to rely on third parties to conduct future clinical trials and preclinical studies for our product candidates. Specifically, we have used and relied on, and intend to continue to use and rely on, medical institutions, clinical investigators, CROs and consultants to conduct our clinical trials in accordance with our clinical protocols and regulatory requirements. These CROs, investigators and other third parties play a significant role in the conduct and timing of these trials and subsequent collection and analysis of data. While we have agreements governing the activities of our third-party contractors, we have limited influence over their actual performance. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs or trial sites fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials or research activities complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP or similar regulations outside the US. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Any third parties conducting our clinical trials or preclinical studies are not and will not be our employees and, except for remedies available to us under our agreements with such third parties, we cannot

guarantee that any such CROs, investigators or other third parties will devote adequate time and resources to such trials or perform as contractually required. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, or otherwise performs in a substandard manner, our clinical trials may be extended, delayed or terminated. In addition, many of the third parties with whom we contract 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 that could harm our competitive position. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash and cash equivalents or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA or foreign regulatory authorities conclude that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned, and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any NDA or similar applications we submit to the FDA or foreign regulatory authorities. Any such delay or rejection could prevent us from commercializing our product candidates.

Our CROs have the right to terminate their agreements with us in the event of an uncured material breach. In addition, some of our CROs and substantially all our clinical trial sites have an ability to terminate their respective agreements with us if it can be reasonably demonstrated that the safety of the subjects participating in our clinical trials warrants such termination.

If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative third parties or do so on commercially reasonable terms. Switching or adding additional CROs, investigators and other third parties involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which could materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, investigators and other third parties, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

We may collaborate with third parties for the development and commercialization of our candidates. We may not succeed in establishing and maintaining collaborative relationships, which may significantly limit our ability to develop and commercialize our product candidates successfully, if at all.

We may seek collaborative relationships for the development and commercialization of our product candidates. If we enter into any collaborative arrangements with any third parties, we will likely have shared or limited control over the amount and timing of resources that our collaborators dedicate to the development or potential commercialization of any product candidates we may seek to develop with them. Our ability to generate product revenue from any collaborations will depend on our collaborators' abilities to successfully perform the functions assigned to them. We cannot predict the success of any collaboration that we enter into.

Collaborations involving our product candidates involve many risks, including:

- collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not properly obtain, maintain, enforce or defend intellectual property or proprietary rights relating to our product candidates or may use our proprietary information inappropriately or in such a way as to expose us to potential litigation or other intellectual property-related proceedings, including proceedings challenging the scope, ownership, validity and enforceability of our intellectual property;
- collaborators may own or co-own intellectual property rights covering our product candidates that result from our collaboration with them, and in such cases, we may not have the exclusive right to commercialize such intellectual property or such product candidates;

- disputes may arise with respect to the ownership of intellectual property developed pursuant to collaborations;
- we may need the cooperation of our collaborators to enforce or defend any intellectual property we contribute to or that arises out of our collaborations, which may not be provided to us;
- collaborators may infringe, misappropriate or otherwise violate the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborators may terminate the collaboration, and, as a result, we may not be able to develop a product candidate or we will have to use our own clinical resources and capital to continue development of the product candidate;
- collaborators may decide not to pursue development and commercialization of any product candidates we develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors, such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial, 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 if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive;
- collaborators with marketing and distribution rights to one or more product candidates may not commit sufficient resources to the marketing and distribution of such product candidates;
- we may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control;
- collaborators may undergo a change of control and the new owners may decide to take the collaboration in a direction that is not in our best interest;
- collaborators may become party to a business combination transaction and the continued pursuit and emphasis on our development or commercialization program by the resulting entity under our existing collaboration could be delayed, diminished or terminated;
- collaborators may become bankrupt, which may significantly delay our research or development programs, or may cause us to lose access to valuable technology, devices, materials, know-how or intellectual property of the collaborator relating to our product candidates;
- key personnel at our collaborators may leave, which could negatively impact our ability to productively work with our collaborators;
- collaborations may require us to incur short- and long-term expenditures, issue securities that dilute our stockholders, or disrupt our management and business;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization or result in delays to development or commercialization of the applicable product candidates; and
- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

For example, in February 2022, the Roche License Agreement under which we exclusively granted to Roche certain rights to develop bemnifosbuvir and certain rights to commercialize bemnifosbuvir outside of the US terminated. As a result, substantially all activities that Roche was conducting in connection with the development and manufacture of bemnifosbuvir, including global manufacture of clinical trial material and certain operations necessary for the conduct of clinical trials, ceased. Substantially all of these activities are necessary for the continued global development of a bemnifosbuvir COV19 product candidate and we are now solely responsible for the conduct and cost of such activities.

We may face significant competition in seeking appropriate collaborations. Business combinations among biotechnology and pharmaceutical companies have resulted in a reduced number of potential collaborators. In addition, the negotiation process is time-consuming and complex, and we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate or delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue.

If we enter into collaborations to develop and potentially commercialize any product candidates, we may not be able to realize the benefit of such transactions if we or our collaborator elect not to exercise the rights granted under the agreement or if we or our collaborator are unable to successfully integrate a product candidate into existing operations. In addition, if our agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator's technology or intellectual property or require us to stop development of those product candidates completely. For example, if the license agreement with Merck was terminated, we would be required to discontinue the development, manufacture and commercialization of ruzasvir in combination with bemnifosbuvir, our lead product candidate for the treatment of HCV, unless we could enter into another agreement with Merck potentially on terms less favorable to us. We may also find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. Any collaborator may also be subject to many of the risks relating to product development, regulatory approval, and commercialization described in this "Risk Factors" section, and any negative impact on our collaborators may adversely affect us.

Data provided by collaborators and others upon which we rely that have not been independently verified could turn out to be false, misleading or incomplete.

We rely on third-party vendors, such as CROs, scientists and collaborators to provide us with significant data and other information related to our programs, preclinical studies or clinical trials and our business. If such third parties provide inaccurate, misleading or incomplete data, our business, prospects and results of operations could be materially adversely affected.

Our employees and independent contractors, including principal investigators, CROs, consultants, vendors and any third parties we may engage in connection with research, development, regulatory, manufacturing, quality assurance and other pharmaceutical functions and commercialization may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

Misconduct by our employees and independent contractors, including principal investigators, CROs, consultants, vendors and any third parties we may engage in connection with research, development, regulatory, manufacturing, quality assurance and other pharmaceutical functions and commercialization, could include intentional, reckless or negligent conduct or unauthorized activities that violate: (i) the laws and regulations of the FDA, and other similar regulatory authorities, including those laws that require the reporting of true, complete and accurate information to such authorities; (ii) manufacturing standards; (iii) data privacy, security, anti-corruption, fraud and abuse and other healthcare laws and regulations; or (iv)

laws that require the reporting of true, complete and accurate financial information and data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws could also involve the improper use or misrepresentation of information obtained in the course of preclinical studies or clinical trials, creation of fraudulent data in preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, 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 comply with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. 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 civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid, other US federal healthcare programs or healthcare programs in other jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

If our CMOs and CROs use hazardous and biological materials in a manner that causes injury or violates applicable law, we may be liable for damages.

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical materials by our CMOs and medical and biological materials by our CROs. Our CMOs and CROs are subject to federal, state and local laws and regulations in the US and in the countries in which they operate governing the use, manufacture, storage, handling and disposal of medical and hazardous materials. Although we believe that our CMOs' and CROs' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of contamination or injury resulting from medical or hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state or federal authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. Generally, we do not have any insurance for liabilities arising from the improper handling of medical and biological or hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, prospects, financial condition or results of operations.

Risks Related to Intellectual Property

If we are unable to obtain, maintain, enforce and adequately protect our intellectual property rights with respect to our technology and product candidates, or if the scope of the patent or other intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and product candidates may be adversely affected.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect our intellectual property and prevent others from duplicating AT-511 (the free base of bemnifosbuvir), bemnifosbuvir and our in-licensed compound ruzasvir and their use or manufacture, or any of our other pipeline product candidates and any future product candidates. Our success depends in large part on our ability to obtain and maintain patent protection in the US and other countries with respect to such product candidates.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patents or patent applications at a reasonable cost or in a timely manner. Although we enter into confidentiality agreements with parties who

have access to confidential or patentable aspects of our research and development output, such as our employees, CROs, consultants, scientific advisors and other contractors, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the US and other jurisdictions are typically not published until 18 months after filing, and some remain so until issued. 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 any patent application related to an invention or product candidate. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

The strength of patents in the pharmaceutical field involves complex legal, factual and scientific questions and can be uncertain. It is possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. The patent applications that we own may fail to result in issued patents with claims that cover our product candidates in the US or in other foreign countries. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if such patents cover our product candidates, third parties may challenge the inventorship, ownership, validity, enforceability or scope of such patents, which may result in such patents being narrowed or invalidated, or being held unenforceable. Our pending and future patent applications may not result in patents being issued which protect our technology or product candidates or which effectively prevent others from commercializing competitive technologies and product candidates. Additionally, any US provisional patent application that we file is not eligible to become an issued patent until, among other things, we file a non-provisional patent application within 12 months of filing the related provisional patent application. If we do not timely file any non-provisional patent application, we may lose our priority date with respect to the provisional patent application and any patent protection on the inventions disclosed in the provisional patent application.

Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates or prevent others from designing around our claims. In addition, no assurances can be given that third parties will not create similar or alternative products or methods that achieve similar results without infringing upon our patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

If the patent applications we hold with respect to our programs or product candidates fail to issue, if the breadth or strength of protection of our current or future issued patents is threatened, or if they fail to provide meaningful exclusivity for our product candidates, it could dissuade companies from collaborating with us to develop product candidates, or threaten our ability to commercialize our current or future product candidates. Several patent applications covering our product candidates have been filed recently by us. We cannot offer any assurances about which, if any, will result in issued patents, the breadth of any such patents or whether any issued patents will be found invalid or unenforceable or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop.

The issuance of a patent is not conclusive as to its inventorship, ownership, scope, validity or enforceability, and our patents may be challenged in courts or patent offices in the US and abroad. In addition, the issuance of a patent does not give us the right to practice the patented invention, as third parties may have blocking patents that could prevent us from marketing our product candidate, if approved, or practicing our own patented technology.

Wide-ranging patent reform legislation in the US, including the Leahy-Smith America Invents Act of 2011 (“Leahy-Smith Act”), may increase the uncertainty of the strength or enforceability of our intellectual property and the cost to defend it. The Leahy-Smith Act includes a number of significant changes to US patent law, including provisions that affect the way patent applications are prosecuted and also affect patent litigation. Under the Leahy-Smith Act, the US transitioned from a “first-to-invent” to a “first-to-file”

system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. This will require us to be prompt going forward during the time from invention to filing of a patent application and to be diligent in filing patent applications, but circumstances could prevent us from promptly filing or prosecuting patent applications on our inventions. The Leahy-Smith Act also enlarged the scope of disclosures that qualify as prior art. Furthermore, if a third-party filed a patent application before effectiveness of applicable provisions of the Leahy-Smith Act, on March 16, 2013, an interference proceeding in the US can be initiated by a third-party to determine if it was the first to invent any of the subject matter covered by the claims of our patent applications. We may also be subject to a third-party preissuance submission of prior art to the US Patent and Trademark Office ("USPTO").

The Leahy-Smith Act created for the first time new procedures to challenge issued patents in the US, including post-grant review, inter partes review and derivation proceedings, which are adversarial proceedings conducted at the USPTO, 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 a priority date of March 16, 2013 or later, which all of our patent filings have, 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 was filed 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 a priority date of March 16, 2013 or later. Post-grant review proceedings can be brought on any ground of challenge, whereas inter partes review proceedings can only be brought to raise a challenge based on published prior art. These adversarial actions at the USPTO include review of patent claims without the presumption of validity afforded to US patents in lawsuits in US federal courts. The USPTO issued a final rule effective November 13, 2018 announcing that it will now use the same claim construction standard currently used in the US federal courts to interpret patent claims in USPTO proceedings, which is the plain and ordinary meaning of words used. If any of our patents are challenged by a third-party in such a USPTO proceeding, there is no guarantee that we will be successful in defending the patent, which would result in a loss of the challenged patent right to us, including loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, 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 product candidates. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us.

As a result of all of the foregoing, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Third-party claims of intellectual property infringement, misappropriation or other violation may result in substantial costs or prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our avoiding actual and allegations of infringement, misappropriation or other violation of the patents and other proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the US, involving patent and other intellectual property rights in the pharmaceutical industry, including patent infringement lawsuits, interferences, oppositions, re-examination, and post-grant and inter partes review proceedings before the USPTO and similar proceedings in foreign jurisdictions, such as oppositions before the EPO. Numerous US and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. Many companies in intellectual property-dependent industries, including the pharmaceutical industry, have employed intellectual property litigation as a means to gain an advantage over their competitors. As the pharmaceutical industry expands and more patents are issued, and as we gain greater visibility and market exposure as a public company, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to composition of matter, drug delivery, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. We cannot guarantee that our technologies, products, compositions and their uses do not or will not infringe, misappropriate or otherwise violate third-party patent or other intellectual property rights. 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 infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Pending patent applications that have been published can, or subject to certain limitations, later present claims in a manner that could cover our product candidates or the use of our product candidates. After issuance, the scope of patent claims remains subject to construction as determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our product candidates. In order to successfully challenge the validity of a US patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such US patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such US patent. If any third-party patents were held by a court of competent jurisdiction to cover the composition of matter of any of our product candidates, the manufacturing process of any of our product candidates or the method of use for any of our product candidates, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, which may not be available at all or on commercially reasonable terms, or until such patents expire.

The legal threshold for initiating litigation or contested proceedings is low, so that even lawsuits or proceedings with a low probability of success might be initiated and require significant resources to defend. Litigation and contested proceedings can also be expensive and time-consuming, and our adversaries in these proceedings may have the ability to dedicate greater resources to prosecuting these legal actions than we can. The risks of being involved in such litigation and proceedings may increase if and as our product candidates near commercialization and as we gain the greater visibility associated with being a public company. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of the merit of such claims. We may not be aware of all intellectual property rights potentially relating to our technology and product candidates and their uses, or we may incorrectly conclude that third-party intellectual property is invalid or that our activities and product candidates do not infringe, misappropriate or otherwise violate such intellectual property. Thus, we do not know with certainty that our technology and product candidates, or our development and commercialization thereof, do not and will not infringe, misappropriate or otherwise violate any third-party's intellectual property.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates and/or harm our reputation and financial results. Defense of these claims, regardless of their merit, could involve substantial litigation expense and could be a substantial diversion of management and employee resources from our business. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products, in the case of claims concerning registered trademarks, rename our product candidates, or obtain one or more licenses from third parties, which may require substantial time and monetary expenditure, and which might be impossible or technically infeasible. Furthermore, 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 and other third parties 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. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and prospects.

A number of companies and universities file and obtain patents in the same area as our products, which are nucleotide prodrugs, and these patent filings could be asserted against us, which may affect our business, and if successful, could lead to expensive litigation, affect the profitability of our products and/or prohibit the sale of a product or its use.

Our product candidates are predominantly nucleotide prodrugs, or nucleotide phosphoramidates. A number of companies and universities have patent applications and issued patents in this general area, including for viral indications, such as, for example, Gilead Pharmasset, LLC.; Gilead Sciences, Inc.; Merck & Co.; Bristol Myers Squibb; F. Hoffmann-La Roche; University of Cardiff; University College Cardiff Consultants; NuCana, plc; Alios Biopharma; Medivir; and others. If any of these companies or universities, or others, assert that a patent it holds is infringed by any of our product candidates or their use or manufacture, we may be drawn into expensive litigation, which may affect our business, take the time of and distract the attention of our employees, and if the litigation is successful, could affect the profitability of our products or prohibit their sale. On June 3, 2019, we received an anonymous third-party Observation filed in connection with our international Patent Cooperation Treaty patent application for our second patent family, which covers the hemisulfate salt form of AT-511, or bemnifosbuvir. The Observation generally challenges the patentability of the hemisulfate salt bemnifosbuvir over the free base AT-511. On August 1, 2019, we filed a response to the Observation describing that the bemnifosbuvir hemisulfate salt of AT-511 is not obvious in view of the AT-511 free base because bemnifosbuvir disproportionately concentrates in the liver over the heart, as shown in vivo in a dog model, which can provide an increased therapeutic effect to treat HCV, and decreased toxicity because hepatitis C is a disease of the liver. Further, while not raised in the response to the Observation, we have now also shown that bemnifosbuvir has a longer half-life and higher concentration in the lung than in the liver in vivo in monkeys, which is relevant to our COVID-19 indication. On August 10, 2020, an anonymous party filed a third-party Observation against our Patent Cooperation Treaty patent application covering a method to treat HCV patients with compensated or decompensated cirrhosis using our drug bemnifosbuvir. The anonymous party asserted that it would have been obvious that the hemisulfate salt of AT-511 (bemnifosbuvir) would be effective to treat HCV-infected cirrhotic patients. We filed a response to the Observation on October 2, 2020, wherein we disagreed for several reasons, including that the hemisulfate salt of AT-511 had not been publicly disclosed at the time of the filing of our method of treatment of cirrhosis application and further noted that it is not straightforward that a treatment for patients with compensated cirrhosis would also be effective for patients with decompensated cirrhosis. Our Patent Cooperation Treaty patent application provides human data that supports the efficacy of using bemnifosbuvir to treat cirrhotic HCV-infected patients. The Observations by anonymous third parties as well as our responses are placed in the file and available to be read and considered by any country examining our respective patent applications. In December 2019, the US Patent Office issued a patent to us covering the composition of matter of bemnifosbuvir. However, other than the foregoing issued US patent, there can be no assurance that the Observations will not adversely affect our ability to obtain issued patents from national-stage filings of such Patent Cooperation Treaty patent applications in any jurisdictions. We may not be aware of patent claims that are currently or may in the future be pending that affect our business by the competitors working in this area. Patent applications are typically published between six and eighteen months from filing, and the presentation of new claims in already pending applications can sometimes not be visible to the public, including to us, for a period of time, or if publicly available, not yet seen by us. We cannot provide any assurance that a third-party practicing in the general area of our technology will not present a patent claim that covers one or more of our products or their methods of use or manufacture at any time, including before or during this registration period. If that does occur, we may have to take steps to try to invalidate such patent or application, and we may either choose not to or may not be successful in such attempt. A license to the patent or application may not be available on commercially reasonable terms or at all.

Our products are subject to The Drug Price Competition and Patent Term Restoration Act of 1984, as amended (also referred to as the Hatch-Waxman Act), in the US, that can increase the risk of litigation with generic companies trying to sell our products, and may cause us to lose patent protection.

Because our clinical candidates are pharmaceutical molecules reviewed by the Center for Drug Evaluation and Research of the FDA, after commercialization they will be subject in the US to the patent

litigation process of the Hatch-Waxman Act, as currently amended, which allows a generic company to submit an ANDA to the FDA to obtain approval to sell our drug using bioequivalence data only. Under the Hatch-Waxman Act, we will have the opportunity to list our patents that cover our drug product or its method of use in the FDA's compendium of "Approved Drug Products with Therapeutic Equivalence Evaluation," sometimes referred to as the FDA's Orange Book.

Currently, in the US, the FDA may grant five years of exclusivity for new chemical entities ("NCEs") for which all of our products may qualify. An NCE is a drug that contains no active moiety that has been approved by the FDA in any other NDA. A generic company can submit an ANDA to the FDA four years after approval of our product. The submission of the ANDA by a generic company is considered a technical act of patent infringement. The generic company can certify that it will wait until the natural expiration date of our listed patents to sell a generic version of our product or can certify that one or more of our listed patents are invalid, unenforceable or not infringed. If the latter, we will have 45 days to bring a patent infringement lawsuit against the generic company. This will initiate a challenge to one or more of our Orange Book-listed patents based on arguments from the generic company that our listed patents are invalid, unenforceable or not infringed. Under the Hatch-Waxman Act, if a lawsuit is brought, the FDA is prevented from issuing a final approval on the generic drug until 30 months after the end of our data exclusivity period, or a final decision of a court holding that our asserted patent claims are invalid, unenforceable or not infringed. If we do not properly list our relevant patents in the Orange Book, do not timely file a lawsuit in response to a certification from a generic company under an ANDA, or if we do not prevail in the resulting patent litigation, we can lose our proprietary protection, and our product can rapidly become generic. Further, even if we do correctly list our relevant patents in the Orange Book, bring a lawsuit in a timely manner and prevail in that lawsuit, the generic litigation may be at a very significant cost to us of attorneys' fees and employee time and distraction over a long period. Further, it is common for more than one generic company to try to sell an innovator drug at the same time, and so we may be faced with the cost and distraction of multiple lawsuits. We may also determine it is necessary to settle the lawsuit in a manner that allows the generic company to enter our market prior to the expiration of our patent or otherwise in a manner that adversely affects the strength, validity or enforceability of our patent.

A number of pharmaceutical companies have been the subject of intense review by the FTC or a corresponding agency in another country based on how they have conducted or settled drug patent litigation, and certain reviews have led to an allegation of an antitrust violation, sometimes resulting in a fine or loss of rights. We cannot be sure that we would not also be subject to such a review or that the result of the review would be favorable to us, which could result in a fine or penalty.

The FTC has brought a number of lawsuits in federal court in the past few years to challenge Hatch-Waxman Act ANDA litigation settlements between innovator companies and generic companies as anti-competitive. As an example, the FTC has taken an aggressive position that anything of value is a payment, whether money is paid or not. Under its approach, if an innovator as part of a patent settlement agrees not to launch or delay launch of an authorized generic during the 180-day period granted to the first generic company to challenge an Orange Book-listed patent covering an innovator drug, or negotiates a delay in entry without payment, the FTC may consider it an unacceptable reverse payment. The pharmaceutical industry argues that such agreements are rational business decisions to dismiss risk and are immune from antitrust attack if the terms of the settlement are within the scope of the exclusionary potential of the patent. In 2013, the US Supreme Court, in a five-to-three decision in FTC v. Actavis, Inc., rejected both the pharmaceutical industry's and FTC's arguments with regard to so-called reverse payments, and held that whether a "reverse payment" settlement involving the exchange of consideration for a delay in entry is subject to an anticompetitive analysis depends on five considerations: (a) the potential for genuine adverse effects on competition; (b) the justification of payment; (c) the patentee's ability to bring about anticompetitive harm; (d) whether the size of the payment is a workable surrogate for the patent's weakness; and (e) that antitrust liability for large unjustified payments does not prevent litigating parties from settling their lawsuits, for example, by allowing the generic to enter the market before the patent expires without the patentee's paying the generic. Furthermore, whether a reverse payment is justified depends upon its size, its scale in relation to the patentee's anticipated future litigation costs, its independence from other services for which it might represent payment, as was the case in Actavis, and the lack of any other convincing justification. The Court held that reverse payment

settlements can potentially violate antitrust laws and are subject to the standard antitrust rule-of-reason analysis, with the burden of proving that an agreement is unlawful on the FTC, leaving to lower courts the structuring of such rule of reason analysis. If we are faced with drug patent litigation, including Hatch-Waxman Act litigation with a generic company, we could be faced with such an FTC challenge based on that activity, including how or whether we settle the case, and even if we strongly disagree with the FTC's position, we could face a significant expense or penalty.

Patent terms may be inadequate to protect our competitive position on our products for an adequate amount of time.

The term of any individual patent depends on applicable law in the country where the patent is granted. In the US, provided all maintenance fees are timely paid, a patent generally has a term of 20 years from its application filing date or earliest claimed non-provisional filing date. Extensions may be available under certain circumstances, but the life of a patent and, correspondingly, the protection it affords is limited. 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. For patents that are eligible for extension of patent term, we expect to seek extensions of patent terms in the US and, if available, in other countries, however there can be no assurance that we will be granted any patent term extension we seek, or that any such patent term extension will provide us with any competitive advantage.

The Hatch-Waxman Act in the US provides for the opportunity to seek a patent term extension on one selected patent for each of our products, and the length of that patent term extension, if at all, is subject to review and approval by the USPTO and the FDA.

In the US, the Hatch-Waxman Act permits one patent term extension of up to five years beyond the normal expiration of one patent per product, which if a method of treatment patent, is limited to the approved indication (or any additional indications approved during the period of extension). The length of the patent term extension is typically calculated as one half of the clinical trial period plus the entire period of time during the review of the NDA by the FDA, minus any time of delay by us during these periods. There is also a limit on the patent term extension to a term that is no greater than fourteen years from drug approval. Therefore, if we select and are granted a patent term extension on a recently filed and issued patent, we may not receive the full benefit of a possible patent term extension, if at all. We might also not be granted a patent term extension at all, because of, for example, failure to apply within the applicable period, failure to apply prior to the expiration of relevant patents or otherwise failure to satisfy any of the numerous applicable requirements. Moreover, the applicable authorities, including the FDA and the USPTO in the US, and any equivalent regulatory authorities in other countries, may not agree with our assessment of whether such extensions are available, may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to obtain approval of competing products following our patent expiration by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. If this were to occur, it could have a material adverse effect on our ability to generate product revenue.

In 1997, as part of the Food & Drug Administration Modernization Act, ("FDAMA"), Congress enacted a law that provides incentives to drug manufacturers who conduct studies of drugs in children. The law, which provides six months of exclusivity in return for conducting pediatric studies, is referred to as the pediatric exclusivity provision. If clinical studies are carried out by us that comply with the FDAMA, we may receive an additional six-month term added to our regulatory data exclusivity period and our patent term extension period, if received, on our product. However, if we choose not to carry out pediatric studies that comply with the FDAMA, or are not accepted by the FDA for this purpose, we would not receive this additional six-month exclusivity extension to our data exclusivity or our patent term extension.

In Europe, supplementary protection certificates are available to extend a patent term up to five years to compensate for patent term lost during regulatory review, and can be extended for an additional six months if data from clinical trials is obtained in accordance with an agreed-upon pediatric investigation plan. Although all countries in Europe must provide supplementary protection certificates, there is no unified legislation among European countries and so supplementary protection certificates must be applied for and granted on a country-by-country basis. This can lead to a substantial cost to apply for and receive these certificates, which may vary among countries or not be provided at all.

If we are unable to obtain licenses from third parties on commercially reasonable terms or at all, 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 other proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties. If we are unable to license such technology, or if we are forced to license such technology on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning or otherwise controlling such intellectual property rights could seek either an injunction prohibiting our sales or 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, thereby giving our competitors and other third parties access to the same technologies licensed to us. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us.

If we are unable to obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may be required to expend significant time and resources to redesign our technology, product candidates or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected technology and product candidates, which could harm our business, financial condition, results of operations and prospects significantly.

Additionally, if we fail to comply with our obligations under any future license agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market, or may be forced to cease developing, manufacturing or marketing, any product that is covered by these agreements or may face other penalties under such agreements. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements, or restrictions on our ability to freely assign or sublicense our rights under such agreements when it is in the interest of our business to do so, 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, or delay or prohibit the further development or commercialization of one or more product candidates that rely on such agreements.

Although we are not currently involved in any relevant litigation, 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 and other third parties may infringe, misappropriate or otherwise violate our or our future licensors' patents, trademarks, copyrights or other intellectual property. As a result, we may need to file infringement, misappropriation or other intellectual property-related claims against third parties. To counter infringement or other unauthorized use, we may be required to file claims on a country-by-country basis, which can be expensive and time-consuming and divert the time and attention of our management and scientific personnel. There can be no assurance that we will have sufficient financial or other resources to file and pursue such claims, which often last for years before they are concluded.

Any claims we assert against third parties could also provoke these parties to assert counterclaims against us alleging that we infringe, misappropriate or otherwise violate their intellectual property. In addition, in a patent infringement proceeding, such parties could counterclaim that the patents we have asserted are invalid or unenforceable, or both. In patent litigation in the US, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone

connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may institute such claims before administrative bodies in the US or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, inter partes review, interference proceedings, derivation proceedings and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). The outcome following legal assertions of invalidity and unenforceability is unpredictable.

In any such proceeding, a court may decide that a patent of ours, or a patent that we in-license, is not valid, is unenforceable and/or is not infringed, or may construe such patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, interpreted narrowly or held unenforceable in whole or in part, could put our patent applications at risk of not issuing, and could limit our ability to assert those patents against those parties or other competitors and 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, which could materially harm our business and negatively affect our position in the marketplace.

Even if we establish infringement, misappropriation or other violation of our intellectual property, the court may decide not to grant an injunction against further such 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 this type of 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 have a material adverse effect on the price of our common stock. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and prospects.

On April 12, 2022, we received notification of a Pre-Grant Opposition from the Controller General of Patents, Designs, and Trademarks at the Indian Patent Office. The Opposition was filed by Sankalp Rehabilitation Trust and challenges our pending patent claims to AT-511 or a pharmaceutically acceptable salt thereof. While we intend to vigorously defend our patent claims on AT-511 and its use to treat hepatitis C, we cannot guarantee that the Indian Patent Office will decide in our favor and allow our patent claims to grant. In addition, Pre-Grant Oppositions in India can proceed very slowly, and therefore this proceeding may not be resolved for several years. Our patent application will not issue as a patent on AT-511 or its use to treat HCV in India unless and until this Pre-Grant Opposition is resolved in our favor. If it is not resolved in our favor, we may not receive a patent on AT-511 in India.

Obtaining and maintaining our 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.

The USPTO, EPO and other patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the US in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay such fees due to non-US patent agencies. While, in many cases, an inadvertent lapse can 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. In such an event, our competitors or other third parties might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

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

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive. Therefore, we may choose not to pursue or maintain protection for certain intellectual property in certain jurisdictions. The requirements for patentability may differ in certain countries, particularly in developing countries. Competitors may use our technologies in jurisdictions where we have not 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 US. 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 changes in foreign intellectual property laws. Additionally, laws of some countries outside of the US and Europe do not afford intellectual property protection to the same extent as the laws of the US 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, may not favor the enforcement of our patents and other intellectual property rights.

This could make it difficult for us to stop the infringement of our patents or the misappropriation or other violation of our other intellectual property rights. A number of foreign countries have stated that they are willing to issue compulsory licenses to patents held by innovator companies on approved drugs to allow the government or one or more third-party companies to sell the approved drug without the permission of the innovator patentee where the foreign government concludes it is in the public interest. India, for example, has used such a procedure to allow domestic companies to make and sell patented drugs without innovator approval. There is no guarantee that patents covering any of our drugs will not be subject to a compulsory license in a foreign country, or that we will have any influence over if or how such a compulsory license is granted. Further, Brazil allows its regulatory agency ANVISA to participate in deciding whether to grant a drug patent in Brazil, and patent grant decisions are made based on several factors, including whether the patent meets the requirements for a patent and whether such a patent is deemed in the country's interest. In addition, several other countries have created laws that make it more difficult to enforce drug patents than patents on other kinds of technologies. Further, under the treaty on the Trade-Related Aspects of Intellectual Property ("TRIPS"), as interpreted by the Doha Declaration, countries in which drugs are manufactured are required to allow exportation of the drug to a developing country that lacks adequate manufacturing capability. Therefore, our drug markets in the US or foreign countries may be affected by the influence of current public policy on patent issuance, enforcement or involuntary licensing in the healthcare area.

In addition, in November 2015, members of the World Trade Organization ("WTO"), which administers TRIPS, voted to extend the exemption against enforcing pharmaceutical drug patents in least developed countries until 2033. We currently have no patent applications filed in least developed countries, and our current intent is not to file in these countries in the future, at least in part due to this WTO pharmaceutical patent exemption.

Furthermore, the WTO is currently considering a waiver of intellectual property rights for COVID-19 vaccines and the US government recently took a stance in support of the waiver. The current proposal is for a temporary waiver of intellectual property rights that cover COVID-19 vaccines, however, the ultimate timing and scope of the waiver, if approved, is unknown. The scope and timing of such waiver will likely be subject to extensive negotiations given the complexity of the matter, which may result in prolonged uncertainty and therefore could adversely affect our business. If a waiver is approved and covers COVID-19 treatments, such as bemnifosbuvir, our ability to successfully commercialize bemnifosbuvir and protect our related technology could be adversely affected.

We rely on our ability to stop others from competing by enforcing our patents, however some jurisdictions may require us to grant licenses to third parties. Such compulsory licenses could be extended to include some of our product candidates, which may limit our potential revenue opportunities.

Many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties, in certain circumstances. For example, compulsory licensing, or the threat of compulsory licensing, of life-saving products and expensive products is becoming increasingly popular in developing countries, either through direct legislation or international initiatives. Compulsory licenses could be extended to include some of our product candidates, if they receive marketing approval, which may limit our potential revenue opportunities. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the US and Europe. Competitors may also use our technologies in jurisdictions where we have not obtained patent protection to develop 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. 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. Furthermore, while we intend to protect our intellectual property rights in major markets for our products where such patent rights exist, 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.

In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may be limited to monetary relief and may be unable to enjoin infringement if a government is the infringer, which could materially diminish the value of the patent.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is either not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with parties who have access to them, such as our employees, CROs, consultants, scientific advisors and other contractors. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. 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. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached and our trade secrets could be disclosed, and we may not have adequate remedies for any such breach. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the US are less willing or unwilling to protect trade secrets. Misappropriation or unauthorized disclosure of our trade secrets or other confidential proprietary information could cause us to lose trade secret protection, impair our competitive position and have a material adverse effect on our business. Additionally, if the steps taken to maintain our trade secrets or other confidential proprietary information are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret or other confidential proprietary information.

Further, we cannot provide any assurances that competitors or other third parties will not otherwise gain access to our trade secrets and other confidential proprietary information or independently discover or develop substantially equivalent technology and processes. If we are unable to prevent disclosure of the trade secrets and other non-patented intellectual property related to our product candidates and technologies to third parties, there is no guarantee that we will have any such enforceable trade secret

protection and we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties, that our employees have wrongfully used or disclosed alleged trade secrets of their former employers, or asserting ownership of what we regard as our own intellectual property.

We have employed, and may in the future employ, individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and independent contractors 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 our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of such individuals' former employers or other third parties. Litigation may be necessary to defend against these 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 our ability to hire personnel, which, in any case of the foregoing, could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Although it is our policy to require all of our employees and consultants to assign their inventions to us, to the extent that employees or consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. We may also be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Our proprietary rights may not adequately protect our technologies and product candidates, and intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make products that are the same as or similar to our product candidates but that are not covered by the claims of our patents;
- others, including inventors or developers of our patented technologies who may become involved with competitors, may independently develop similar technologies that function as alternatives or replacements for any of our technologies without infringing, misappropriating or otherwise violating our intellectual property rights;
- we might not have been the first to conceive and reduce to practice the inventions covered by our patents or patent applications;
- we might not have been the first to file patent applications covering certain of our inventions;
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third-party may subsequently file a patent covering such intellectual property;
- our pending patent applications might not result in issued patents;
- there might be prior public disclosures that could invalidate our patents;
- our issued patents may not provide us with any commercially viable products or competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors or other third parties;

- the Supreme Court of the US, other US federal courts, Congress, the USPTO or similar foreign authorities may change the standards of patentability and any such changes could narrow or invalidate, or change the scope of, our patents;
- patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time;
- our competitors or other third parties might conduct research and development activities in countries where we do not have patent rights, or in countries where research and development safe harbor laws exist, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- ownership, validity or enforceability of our patents or patent applications may be challenged by third parties; and
- the patents or pending or future applications of third parties, if issued, may have an adverse effect on our business.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Risks Related to Employee Matters, Managing Growth and Other Risks Related to Our Business

We will need to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

We expect to experience significant growth over time in the number of our employees and the scope of our operations, particularly in the areas of product candidate development, regulatory and clinical affairs and sales, marketing and distribution. To manage our growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team, as a group, in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. As we expand our company, we may have difficulty identifying, hiring and integrating new personnel. Future growth would impose significant additional responsibilities on our management, including but not limited to:

- the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors; and
- maintaining our operational, financial and management controls, reporting systems and procedures.

Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow product revenues, if any, could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize any approved products and compete effectively will depend, in part, on our ability to effectively manage any future growth.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services, including substantially all aspects of clinical trial conduct and execution, and manufacturing. There can be no assurance that the services of independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by

independent organizations, advisors or consultants is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval of our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing independent organizations, advisors or consultants or find other competent outside independent organizations, advisors and consultants on economically reasonable terms, or at all. If we are not able to effectively expand our organization by hiring new employees and expanding our groups of advisors and consultants, or we are not able to effectively maintain or obtain facilities to accommodate this expansion, we may not be able to successfully implement the tasks necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our research, development and commercialization goals.

Many of the biotechnology and pharmaceutical companies that we compete against for qualified personnel and consultants have greater financial and other resources, different risk profiles and a longer history in the industry than we do. If we are unable to continue to attract and retain high-quality personnel and consultants, the rate and success at which we can discover and develop product candidates and operate our business will be limited.

We only have a limited number of employees to manage and operate our business.

As of February 20, 2023, we had 70 full-time employees. Our focus on the clinical development of product candidates in two distinct disease indications requires us to manage and operate our business in a highly efficient manner. We cannot assure you that we will be able to hire and/or retain adequate staffing levels to develop our product candidates or run our operations and/or to accomplish all of the objectives that we otherwise would seek to accomplish.

If we lose key management or scientific personnel, cannot recruit qualified employees, directors, officers or other significant personnel or experience increases in our compensation costs, our business may materially suffer.

We are highly dependent on our officers, directors and key employees. Due to the specialized knowledge each of our officers, directors and key employees possesses with respect to our product candidates and our operations, the loss of service of any of one or more of our officers, directors or key employees could seriously delay, harm or prevent the planning and execution of clinical trials and other key activities required for the successful advancement of our business. Although we have employment agreements with certain of executive officers, in general, these agreements do not prevent our executive officers from terminating their employment with us at any time.

We do not carry key person life insurance on any officers or directors.

In addition to retaining the continued service of our officers, directors and key employees, our future success and growth will depend in part on our ability to identify, hire and retain additional personnel.

Our ability to identify, hire and retain additional personnel and, if necessary, replace departed executive officers and key employees may be difficult or costly 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 discover or otherwise identify and develop product candidates and gain regulatory 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 effectively incentivize these additional key personnel 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. In addition, 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 engaged by entities other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to develop and commercialize product candidates will be limited.

Many of our key employees are vested in a substantial amount of our common stock or options to purchase our common stock. Our employees, including our key employees, may be more likely to leave us if the shares they own have significantly fluctuated in value relative to the original purchase prices of

the shares, or if the exercise prices of the options that they hold are significantly below or above the market price of our common stock.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and share price.

The global economy, including credit and financial markets, has experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, increases in interest rates, increases in inflation rates and uncertainty about economic stability. For example, the COVID-19 pandemic resulted in widespread unemployment, economic slowdown and extreme volatility in the capital markets. Similarly, the current conflict between Ukraine and Russia has created extreme volatility in the capital markets and is having further global economic consequences including but not limited to those related to the supply of energy, agricultural products and other essential commodities. These conditions may make any necessary debt or equity financing more difficult to obtain in a timely manner or on favorable terms, more costly or more dilutive. Political unrest, such as the current situation with Ukraine and Russia, may also cause volatility and disruption in the global economy. In addition, there is a risk that one or more of our CROs, suppliers, CMOs or other third-party providers may not survive an economic downturn. As a result, our business, results of operations and price of our common stock may be adversely affected.

The continuing impact of "Brexit" may have a negative effect on our business.

Since the end of the Brexit transition period on January 1,2021, Great Britain (England, Scotland and Wales) has not been directly subject to EU laws, however under the terms of the Ireland/Northern Ireland Protocol, EU laws generally apply to Northern Ireland. The EU laws that have been transposed into UK law through secondary legislation remain applicable in Great Britain. However, under the Retained EU Law (Revocation and Reform) Bill 2022, which is currently before the UK parliament, any retained EU law not expressly preserved and "assimilated" into domestic law or extended by ministerial regulations (to no later than June 23, 2026) will automatically expire and be revoked by December 31, 2023. In addition, new legislation such as the CTR is not applicable in Great Britain. The UK government has passed the Medicines and Medical Devices Act 2021, which introduces delegated powers in favor of the Secretary of State or an 'appropriate authority' to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices.

The EU-UK Trade and Cooperation Agreement ("TCA"), came into effect on January 1, 2021. The TCA includes provisions affecting pharmaceutical businesses (including on customs and tariffs). In addition, there are some specific provisions concerning pharmaceuticals. These include the mutual recognition of GMP inspections of manufacturing facilities for medicinal products and GMP documents issued. The TCA does not, however, contain wholesale mutual recognition of UK and EU pharmaceutical regulations and product standards, and it can be expected that there may be divergent local requirements in the UK from the EU in the future, which may impact clinical and development activities that occur in the UK in the future. Similarly, clinical trial submissions and data for activity in the UK will not be able to be bundled with those of EU countries within the EMA Clinical Trial Information System ("CTIS"), adding further complexity, cost and potential risk to future clinical and development activity in the UK. Significant political and economic uncertainty remains about how much the relationship between the UK and EU will differ as a result of the UK's withdrawal.

The long term effects of Brexit on our business in the UK, the EU and worldwide will depend on the effects of the implementation and application of the TCA and any other relevant agreements between the UK and the EU. As of January 1, 2021, the MHRA is the UK's standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales, and Scotland, together, Great Britain; broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA.

These developments have had and may continue to have a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. In particular, it could also lead to a period of considerable uncertainty in relation to the UK financial and banking markets, as well as on the regulatory process in the UK and in Europe. As a result of this uncertainty, global financial markets could experience significant volatility, which could adversely affect the market price of our common stock. Asset valuations, currency exchange rates, and credit ratings may also be subject to increased market volatility. Lack of clarity about future UK laws and regulations as the UK determines which EU rules and regulations to replace or replicate after withdrawal, including financial laws and regulations, tax and free trade agreements, intellectual property rights, data protection laws, supply chain logistics, environmental, health, and safety laws and regulations, immigration laws, and employment laws, could decrease foreign direct investment in the UK, increase costs, depress economic activity, and restrict our access to capital. If the UK and the EU are unable to negotiate acceptable withdrawal terms or if other EU member states pursue withdrawal, barrier-free access between the UK and other EU member states or among the EEA overall could be diminished or eliminated.

As a result of Brexit and new regulatory regimes, we may also face new regulatory costs and challenges that could have an adverse effect on our operations. In addition, currency exchange rates between the pound sterling, the euro and the US dollar have already been, and may continue to be, affected by Brexit.

Risks Related to Our Common Stock

Our principal stockholders and management own a significant percentage of our shares of common stock and could exert significant influence over matters subject to stockholder approval.

Our executive officers, directors, and >5% stockholders beneficially own a significant percentage of our common stock as of December 31, 2022. Therefore, these stockholders may, if acting together, have the ability to influence us through this ownership position. These stockholders may be able to determine matters requiring stockholders approval. For example, these stockholders may be able to control elections of directors, or influence amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our shares of common stock that you may feel are in your best interest as one of our stockholders.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline, even if our business is doing well.

The trading market for our common stock is influenced by the research and reports that industry or securities analysts publish about us or our business. We currently have limited research coverage by securities and industry analysts. If any of the analysts who cover us, or may cover us, downgrades our common stock or issues an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our preclinical studies or clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline as it did following the downgrades by covering analysts in the fourth quarter of 2021 following our report on the data from the Phase 2 MOONSONG clinical trial, which failed to meet the primary study endpoint in the overall patient population and other events. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Provisions in our restated certificate of incorporation and restated bylaws and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our restated certificate of incorporation and our amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions may also limit the price that investors are 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 include those establishing:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from filling vacancies on our board of directors;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of the holders of at least two-thirds of the shares entitled to vote at an election of directors to adopt, amend or repeal our bylaws or repeal the provisions of our restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer, the president or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

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.

Our restated certificate of incorporation designates specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us.

Our restated certificate of incorporation, specifies that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions involving claims brought against us by stockholders, other than suits brought to enforce any liability or duty created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction and any action that the Court of Chancery of the State of Delaware has dismissed for lack of subject matter jurisdiction, which may be brought in another state or federal court sitting in the State of Delaware. Our restated certificate of incorporation also specifies that unless we consent in writing to the selection of an alternate forum, the federal district courts of the US shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933. Any person or entity purchasing or otherwise acquiring any interest in shares of

our capital stock shall be deemed to have notice of and to have consented to the provisions of our restated certificate of incorporation described above.

We believe this provision benefits us by providing increased consistency in the application of Delaware law by chancellors particularly experienced in resolving corporate disputes or federal judges experienced in resolving Securities Act disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi-forum litigation. However, the provision may have the effect of discouraging lawsuits against our directors, officers, employees and agents as it may limit any stockholder's ability to bring a claim in a judicial forum that such stockholder finds favorable for disputes with us or our directors, officers, employees or agents. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our restated certificate of incorporation to be inapplicable or unenforceable in such action. If a court were to find the choice of forum provision contained in our restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business, financial condition or results of operations.

General Risk Factors

Raising additional capital may cause additional dilution to our stockholders, restrict our operations, require us to relinquish rights to our technologies or product candidates, and could cause our share price to fall.

Until such time, if ever, as we can generate substantial revenue from product sales, we may finance our cash needs through a combination of equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our operations, our ability to take specific actions, such as incurring additional debt, making capital expenditures, declaring dividends, redeeming our stock, making certain investments and engaging in certain merger, consolidation or asset sale transactions, among other restrictions. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required 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 through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Weakening patent laws and enforcement by courts and other authorities in the US and other jurisdictions may impact our ability to protect our patents.

The US Supreme Court and lower courts have issued opinions in patent cases in the last few years that many consider may weaken patent protection in the US, either by narrowing the scope of patent protection available in certain circumstances, holding that certain kinds of innovations are not patentable or generally otherwise making it easier to invalidate patents in court. Additionally, there have been recent proposals for additional changes to the patent laws of the US and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the US Congress, the US courts, the USPTO and the relevant law-making and other 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 and defend our existing patents and patents that we might obtain in the future.

The laws of some foreign jurisdictions do not protect intellectual property rights to the same extent as in the US and many companies have encountered significant difficulties in protecting and defending such

rights in foreign jurisdictions. If we encounter such difficulties in protecting or are otherwise precluded from effectively protecting our intellectual property rights in foreign jurisdictions, our business prospects could be substantially harmed. For example, we have been notified that a pre-grant opposition has been filed with the Controller General of Patents, Designs and Trademarks at the Indian Patient Office. While we intend to defend our patent claims for AT-511, we cannot provide any assurance that we will succeed or that the Indian patent office will allow the patent claims to grant. If so, uncertainties resulting from the initiation and continuation of such proceedings could have a material adverse effect on our ability to compete in the marketplace. The cost of foreign adversarial proceedings can also be substantial, and in many foreign jurisdictions, the losing party must pay the attorney fees of the winning party.

We may engage in acquisitions or strategic collaborations that could disrupt our business, cause dilution to our stockholders, reduce our financial resources, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

In the future, we may enter into transactions to acquire other businesses, products or technologies or enter into strategic collaborations, including licensing. If we do identify suitable acquisition or collaboration candidates, we may not be able to complete such acquisitions or collaborations on favorable terms, or at all. Any acquisitions or collaborations may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors, and we may never realize the anticipated benefits of such acquisitions or collaborations. 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 or collaboration that are not covered by the indemnification we may obtain from the seller or our collaborator. In addition, we may not be able to successfully integrate any acquired personnel, technologies and operations into our existing business in an effective, timely and non-disruptive manner. Acquisitions or collaborations may also divert management attention from day-to-day responsibilities, lead to a loss of key personnel, increase our expenses and reduce our cash and cash equivalents available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or collaborations or the effect that any such transactions might have on our operating results.

We or the third parties upon whom we depend may be adversely affected by natural disasters or pandemics and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters (including, but not limited to earthquakes, fires, storms, floods, droughts, and extreme temperatures) or pandemics, other than or in addition to COVID-19, could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition and prospects. Climate change may increase the frequency or intensity of such events. Moreover, climate change may result is various chronic changes in the physical environment, such as changes in temperature or precipitation patterns or sea-level rise, that may also have an adverse impact on our operations. If a natural disaster, power outage, pandemic, such as the COVID-19 pandemic, or other event occurred that prevented us from using all or a significant portion of our headquarters or the virtual network capabilities upon which our employees depend to collaborate and access critical business records, that damaged critical infrastructure, such as the manufacturing facilities on which we rely, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business.

Increased attention to, and evolving expectations for initiatives could increase our costs, harm our reputation, or otherwise adversely impact our business.

Companies across industries are facing increasing scrutiny from a variety of stakeholders related to their ESG and sustainability practices. Expectations regarding voluntary ESG initiatives and disclosures may result in increased costs (including but not limited to increased costs related to compliance, stakeholder engagement, contracting and insurance), enhanced compliance or disclosure obligations, or other adverse impacts to our business, financial condition, or results of operations.

While we may at times engage in voluntary initiatives (such as voluntary disclosures, certifications, or goals, among others) to improve the ESG profile of our Company and/or products, such initiatives may be costly and may not have the desired effect. Moreover, we may not be able to successfully complete such initiatives due to factors that are within or outside of our control. Even if this is not the case, our actions may subsequently be determined to be insufficient by various stakeholders, and we may be subject to investor or regulator engagement on our ESG efforts, even if such initiatives are currently voluntary.

Certain market participants, including major institutional investors and capital providers, use third-party benchmarks and scores to assess companies' ESG profiles in making investment or voting decisions. Unfavorable ESG ratings could lead to increased negative investor sentiment towards us or our industry, which could negatively impact our share price as well as our access to and cost of capital. To the extent ESG matters negatively impact our reputation, it may also impede our ability to compete as effectively to attract and retain employees or customers, which may adversely impact our operations.

In addition, we expect there will likely be increasing levels of regulation, disclosure-related and otherwise, with respect to ESG matters. For example, the SEC has published proposed rules that would require companies to provide significantly expanded climate-related disclosures in their periodic reporting, which may require us to incur significant additional costs to comply, including the implementation of significant additional internal controls processes and procedures regarding matters that have not been subject to such controls in the past, and impose increased oversight obligations on our management and board of directors. These and other changes in stakeholder expectations will likely lead to increased costs as well as scrutiny that could heighten all of the risks identified in this risk factor. Additionally, many of our customers and suppliers may be subject to similar expectations, which may augment or create additional risks, including risks that may not be known to us.

Litigation against us could be costly and time-consuming to defend and could result in additional liabilities.

We may from time to time be subject to legal proceedings and claims that arise in the ordinary course of business or otherwise, such as claims brought by our customers or third parties in connection with commercial disputes and employment claims made by our current or former employees. Claims may also be asserted by or on behalf of a variety of other parties, including government agencies, patients or vendors of our customers, or stockholders. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities.

Any litigation involving us may result in substantial costs, operationally restrict our business, and may divert management's attention and resources, which may seriously harm our business, overall financial condition and results of operations. Insurance may not cover existing or future claims, be sufficient to fully compensate us for one or more of such claims, or continue to be available on terms acceptable to us. A claim brought against us that is uninsured or underinsured could result in unanticipated costs, thereby adversely impacting our results of operations and resulting in a reduction in the trading price of our stock.

The market price of our common stock has been volatile and may fluctuate substantially.

Our stock price has been and is likely to remain volatile. Extreme fluctuations have occurred in our stock price with closing prices in 2021 ranging from a high of $88.44 on February 8, 2021 to a low of $7.67 on November 23, 2021 and in 2022, from a high of $9.19 on January 3, 2022 to a low of $4.35 on December 28, 2022.

The stock market in general, The Nasdaq Global Select Market and biopharmaceutical companies in particular have experienced extreme volatility in trading volume that exacerbates, is disproportionate to or in some cases has been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at a profit. The market price for our common stock may be influenced by many factors, including but not limited to:

- the success of competitive products or technologies;
- actual or expected changes in our growth rate relative to our competitors;
- results of our ongoing, planned or any future preclinical studies, clinical trials or clinical development of our product candidates or those of our competitors;

- unanticipated serious safety concerns related to the use of our product candidates;
- developments related to our existing or any future collaborations;
- developments concerning our manufacturers or our manufacturing plans;
- our inability to obtain adequate product supply for any approved product or inability to do so at acceptable prices;
- regulatory actions with respect to our product candidates or our competitors' products and product candidates;
- regulatory or legal developments in the US and other countries;
- development of third-party product candidates that may address our markets and make our product candidates less attractive;
- changes in physician, hospital or healthcare provider practices that may make our product candidates less useful;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- our failure to commercialize our product candidates;
- announcements by us, our partners or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- developments or disputes concerning patent applications, issued patents or other intellectual property or proprietary rights;
- the recruitment or departure of key scientific or management personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- changes in accounting practices;
- the trading volume of our common stock;
- our cash, cash equivalents and marketable securities position;
- our ability to effectively manage our growth;
- sales of our common stock by us or our stockholders in the future;
- publication of research reports about us or our industry, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- ineffectiveness of our internal controls;
- significant lawsuits, including intellectual property or stockholder litigation;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or expected changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- actual or anticipated variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;

- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions, including rising inflation and interest rates; and
- the other factors described in this “Risk Factors” section.

Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company’s securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management’s attention and resources, which would harm our business, financial condition and results of operations.

If we fail to maintain effective internal control over financial reporting and effective disclosure controls and procedures, we may not be able to accurately report our financial results in a timely manner or prevent fraud, which may adversely affect investor confidence in our company.

We are required to comply with the SEC’s rules implementing Sections 302 and 404 of the Sarbanes-Oxley Act, which require management to certify financial and other information in our quarterly and annual reports and provide an annual management report on the effectiveness of controls over financial reporting. In addition, we are required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm and our independent registered public accounting firm is required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404 for the year ending December 31, 2022. Our independent registered public accounting firm may issue a report that is adverse in the event material weaknesses have been identified in our internal control over financial reporting.

To comply with the requirements of Section 404, we have undertaken and will need to undertake additional actions, such as implementing new internal controls and procedures and hiring additional accounting or internal audit staff. We will need to continue to dedicate internal resources, engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing whether such controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Testing and maintaining internal control can divert our management’s attention from other matters that are also important to the operation of our business. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. When evaluating our internal control over financial reporting, we may identify material weaknesses that we may not be able to remediate in time to meet the applicable deadline imposed upon us for compliance with the requirements of Section 404. If we identify any material weaknesses in our internal controls over financial reporting or we are unable to comply with the requirements of Section 404 in a timely manner or assert that our internal control over financial reporting is effective, or if our independent registered public accounting firm is unable to express an opinion as to the effectiveness of our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports. As a result, the market price of our common stock could be materially adversely affected.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Exchange Act. We are continuing to refine our disclosure controls and procedures to provide reasonable assurance that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of

the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, is likely to be your sole source of gain.

We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain all available funds and future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. As a result, capital appreciation, if any, of our common stock is likely to be your sole source of gain on an investment in our common stock for the foreseeable future.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

Our principal office is located at 225 Franklin Street, Boston, Massachusetts, where we lease 17,544 square feet of office space. We lease this space under a sublease agreement, with the term January 1, 2022 through December 31, 2026. We believe that our facilities are sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings.

We are not subject to any material legal proceedings.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Certain Information Regarding the Trading of Our Common Stock

Our common stock has been listed on The Nasdaq Global Select Market under the symbol "AVIR" since October 30, 2020.

Holders of Our Common Stock

As of February 25, 2023 there were 21 stockholders of record of our common stock, which does not reflect stockholders whose shares were held in nominee or street name by brokers.

Dividends

We have never declared or paid any cash dividends on our common stock. We currently intend to retain all available funds and any future earnings to fund the development and expansion of our business, and therefore do not anticipate paying cash dividends in the foreseeable future. Any future determination to pay dividends will be at the discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements, business prospects, contractual arrangements, any limitations on payment of dividends present in any future debt agreements and other factors that our board of directors may deem relevant, and will be subject to the restrictions contained in any future financing instruments.

Use of Proceeds

On November 3, 2020, we completed the initial public offering ("IPO") of our common stock pursuant to which we issued and sold 14,375,000 shares of our common stock at a price to the public of $24.00 per share.

All shares issued and sold in the initial public offering were registered under the Securities Act pursuant to a Registration Statement on Form S-1 (File No.333-249404), as amended ("Registration Statement"), declared effective by the SEC on October 29, 2020.

We received net proceeds of approximately $317.6 million after deducting underwriting discounts and commissions and offering expenses.

The net proceeds from our IPO have been invested primarily in money market accounts and marketable securities. There has been no material change in the expected use of the net proceeds from our IPO as described in our Prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on October 29, 2020.

Stock Performance Graph

The performance graph compares the performance of our common stock to the S&P 500 Index and to the Nasdaq Biotechnology Index from October 30, 2020 (the first date that shares of our common stock were publicly traded) through December 31, 2022. The comparison assumes $100 was invested in our common stock and in each of the foregoing indices after the market closed on October 30, 2020, and it assumes reinvestment of dividends, if any. The stock price performance included in this graph is not necessarily indicative of, nor is it intended to forecast, future stock price performance.

The following performance graph and related information is furnished and shall not be deemed to be "soliciting material" or to be "filed" with the SEC for purposes of Section 18 of the Exchange Act, nor shall such information be deemed incorporated by reference into any filings under the Exchange Act or the Securities Act, except to the extent that we specifically incorporate it by reference into such filing.

Item 6. Reserved

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our financial statements and the related notes to those statements included elsewhere in this Annual Report on Form 10-K. In addition to historical financial information, the following discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results and timing of selected events may differ materially from those anticipated in these forward-looking statements as a result of many factors, including those discussed in Part I, Item 1A, "Risk Factors" and elsewhere in this Annual Report on Form 10-K. See "Special Note Regarding Forward-Looking Statements."

Overview

We are a clinical-stage biopharmaceutical company focused on discovering, developing, and commercializing antiviral therapeutics to improve the lives of patients suffering from serious viral infections. We are developing our lead product candidate, bemnifosbuvir, for the treatment of COVID-19, the disease caused by infection with SARS-CoV-2 and its variants. We are also developing bemnifosbuvir in combination with ruzasvir for the treatment of HCV.

COVID-19 has caused a global health crisis resulting in millions of deaths and lingering medical issues for many survivors. While there have been many rapid advances in the prevention and treatment of COVID-19, due to the limitations of the current vaccine and treatment options, there remains a significant unmet medical need for large numbers of high-risk individuals both in the US and globally. Our COVID-19 strategy, centered on the development of bemnifosbuvir as a monotherapy and potentially as a part of a COVID-19 therapy that combines bemnifosbuvir with another antiviral agent and focuses on these high-risk patients for whom current vaccines and treatments remain inadequate. Our goal is to deliver a safe, effective, and convenient treatment option for individuals that remain vulnerable to hospitalization and death as a result of infection with SARS-CoV-2.

Even with the availability of vaccines and therapeutics, COVID-19 is the third leading cause of mortality in the US after only heart disease and cancer. As of February 15, 2023, the CDC reported that more than 400 persons a day are dying in the US from COVID-19 or related complications. More than 75% of these persons are 65 years and older. Additionally, it has been reported as recently as February 15, 2023, persons 60 years and older account for ~70 % of current US hospitalizations associated with COVID-19.

While the US government has recently announced plans to end the declaration of a public health emergency associated with COVID-19, COVID-19 is expected to remain a serious endemic threat for an indefinite future period. The reasons contributing to the likelihood of COVID-19 remaining an endemic threat include: (1) viral transmission before symptom onset; (2) uneven global rollout of vaccinations; (3) ongoing vaccine hesitancy; (4) limited duration of immunity conferred by both natural infection and vaccination; (5) limited vaccine efficacy against certain SARS-CoV-2 variants; (6) limitations of current oral antivirals such as drug-drug interactions, safety concerns and tolerability; (7) uncertain impact of vaccines on transmission; (8) continuing evolution of the virus evading endogenous and vaccine-induced immunity; and (9) diminution of virus transmission mitigation behaviors, such as wearing masks and social distancing.

The continued emergence of SARS-CoV-2 variants that may have greater transmissibility and may cause more severe disease, combined with the diminution of virus mitigation behaviors among others in the general population, together with the consequences that are expected to associate with the end of the public health emergency leave patients for whom current therapeutics are limited particularly vulnerable to the virus and related disease. In view of these factors, we are developing bemnifosbuvir as a potential therapy to meet the needs of these vulnerable patients.

As COVID-19 continues to persist as a serious global endemic disease, we believe that the COVID-19 therapeutic market will remain a multi-billion-dollar opportunity for many years to come with the US continuing to comprise the most significant commercial market. In the US, we anticipate that the COVID-19 commercial market will soon transition from a single government payer to more traditional payer channels such as Medicare, Medicaid and private commercial insurance. We anticipate a major

consideration for determining reimbursement by these third party payers will be a cost/value analysis that is driven in part by the economic burden of hospitalization, especially for at-risk populations.

Bemnifosbuvir

We utilized our team's expertise and experience, gained from decades of developing innovative antiviral treatments, to design bemnifosbuvir, an investigational, proprietary, potent, and selective, nucleotide polymerase inhibitor, which may be developed as each of a monotherapy and in combination with other antiviral agents. Bemnifosbuvir (AT-527) has been derived from our internal discovery program that combines unique nucleotide scaffolds with novel double prodrugs for the purpose of inhibiting the enzymes central to viral replication. Utilizing this double prodrug moiety approach, we believe that we have been able to maximize formation of the active metabolite of bemnifosbuvir thereby creating an oral antiviral product candidate that is designed to be preventing replication of ssRNA viruses while avoiding toxicity to host cells. Additionally, in nonclinical studies we have demonstrated that bemnifosbuvir has a unique mechanism of action that includes both RdRp chain termination and inhibition of the NiRAN of the SARS-CoV-2 virus and variants. By targeting these highly conserved sites through this unique dual mechanism of action, bemnifosbuvir has the potential to create a high barrier to resistance. Additionally, in *in vitro* studies we have conducted, bemnifosbuvir maintained its antiviral activity across COVID-19 VOCs, including all Omicron subvariants tested.

COVID-19 Clinical Studies

In November 2022, we initiated SUNRISE-3, a global, multicenter, randomized, double-blind, placebo-controlled Phase 3 clinical trial. SUNRISE-3 is evaluating bemnifosbuvir (550 mg BID for five days) in at least 1500 high-risk non-hospitalized patients with mild or moderate COVID-19. The trial will be conducted at clinical trial sites in the US, Europe, Japan, and other regions of the world. The patient population will consist of those at the highest risk for disease progression, including patients ≥ 80 years old, patients ≥ 65 years old with one or more major risk factors, and immunocompromised patients ≥ 18 years old, all regardless of COVID-19 vaccination status.

SUNRISE-3 is designed to evaluate bemnifosbuvir as monotherapy (primary analysis) but will also explore the effect of combination therapy in a smaller sub-set of patients who receive an antiviral drug along with bemnifosbuvir (secondary analysis). The trial will include two populations derived from the type of SOC received: 1) "supportive care population" (those patients who do not qualify for an approved antiviral treatment or where antivirals are not locally available) which will assess bemnifosbuvir given as monotherapy (primary analysis) and 2) "combination antiviral population" which will assess combination therapy if the SOC includes treatment with other compatible antiviral drugs against COVID-19 (secondary analysis). Patients are being randomized 1:1 to receive either bemnifosbuvir 550 mg BID plus locally available SOC or placebo BID plus locally available SOC for five days.

The primary endpoint of the SUNRISE-3 study is all-cause hospitalization or death through Day 29 in at least 1,300 patients in the supportive care population and is powered to detect a clinically meaningful reduction in hospitalization/death versus placebo in this population. By enriching the patients enrolling in the trial with those who are at the highest risk for disease progression, we are targeting rates of hospitalization/death of ~4-6%. An interim analysis will be conducted by a DSMB after 60% patient enrollment in the arm of the study enrolling the supportive care population. Secondary endpoints in each of the supportive care patient population and the combination antiviral population include COVID-19 complications, medically attended visits, symptom rebound/relapse and viral load rebound.

In parallel to conducting our SUNRISE-3 clinical trial, we are engaging in efforts to discover a protease inhibitor product candidate that we may combine with bemnifosbuvir for the treatment of specific COVID-19 patient populations that are unable to mount immune response and require combination therapy. We have conducted *in vitro* studies that have demonstrated an additive antiviral effect when bemnifosbuvir was combined with antivirals from the protease inhibitor class, including nirmatrelvir. The data that we anticipate obtaining from the SUNRISE-3 clinical trial in the subset of patients who receive combination therapy will be, we believe, the first clinical data evaluating the combination of bemnifosbuvir and certain other currently authorized antiviral treatments.

Combination Therapy

Combination therapy utilizing multiple direct acting antivirals with differing mechanisms of action is an established strategy that has been historically successful in treating many life-threatening viral diseases, including HIV, HBV and HCV. Nucleos(t)ide analogs are the backbone of many of these successful combination therapies. Advantageously, drug combinations can simultaneously target multiple points in the viral replication cycle with the effect of increasing antiviral activity and can also combat resistance that may develop over time with use of single agent drugs.

Hepatitis C Virus (HCV) Clinical Studies

For the treatment of chronic HCV infection, we are advancing the combination of bemnifosbuvir and ruzasvir, an investigational NS5A inhibitor. Approximately 58 million people globally, including ~2.4 million in the US, are living with chronic HCV infection. The WHO reports a global incidence of 1.5 million cases per year and 399,000 deaths per year. The US HCV prevalence is expected to remain constant over the coming years as rising HCV incidence offsets the number of new patients treated.

We believe that the combination of bemnifosbuvir and ruzasvir has the potential to improve upon the current standard of care by offering a differentiated short duration, pan-genotypic protease-sparing regimen for HCV-infected patients with or without cirrhosis.

During the second quarter of 2023, we plan to initiate enrollment of a Phase 2 clinical trial of bemnifosbuvir in combination with ruzasvir in treatment-naïve, HCV-infected patients either without cirrhosis or with compensated cirrhosis. This study is designed to evaluate the safety and efficacy of the pan-genotypic combination consisting of 550 mg QD of bemnifosbuvir and 180 mg QD of ruzasvir after eight weeks of treatment. Approximately 280 HCV-infected, treatment-naïve patients across all genotypes, including a lead-in cohort of approximately 60 patients are expected to be enrolled in this Phase 2 clinical trial. The primary endpoints of the study are safety and sustained virologic response (SVR) at Week 12 post-treatment. Other virologic endpoints include virologic failure, SVR at Week 24 post-treatment and resistance.

Dengue and RSV

In February 2023, after advancing AT-752 to a Phase 2 clinical trial, we have determined not to pursue further clinical development of AT-752 for the treatment and prophylaxis of dengue. This action was taken due to the long timelines anticipated for patient enrollment, expected clinical operational challenges, including the challenge of successfully administering an antiviral very shortly after infection which is not feasible with the current diagnostic tests, and estimated resource burdens, including substantial costs, associated with the further clinical development of an antiviral for each of the treatment and prophylaxis of dengue.

We have also recently have determined not to further pursue further our discovery efforts to identify a product candidate for the treatment of respiratory syncytial virus (RSV). This action was taken to facilitate enhanced focus of our management team and to deploy our other resources on those therapeutic indications where our programs are more advanced.

Financial Resources

We believe we are well capitalized to advance our current programs. We had $646.7 million in cash, cash equivalents and marketable securities at December 31, 2022. Based on our current plans, we anticipate these financial resources will allow us to advance our current and planned clinical programs to and through key inflection points and to fund our activities into 2026.

Roche License Agreement

In October 2020, we entered into the Roche License Agreement, with F. Hoffmann-La Roche Ltd and Genentech, Inc. in connection with the global development, manufacture and commercialization of the Compounds, Products, and Companion Diagnostics. Subject to the terms and conditions of the Roche License Agreement, Roche and we jointly developed bemnifosbuvir for COVID-19 on a worldwide-basis and equally shared the costs associated with such development activities.

As partial consideration of the rights we granted to Roche under the Roche License Agreement, Roche paid us an upfront payment of $350 million in November 2020. Additionally, upon realization of a development milestone in June 2021, we received an additional $50 million from Roche.

On February 10, 2022 the Roche License Agreement terminated following the receipt of notice of termination from Roche in November 2021. Our obligations to share costs with Roche also ended at that time. As a result of the termination of the Roche License Agreement, we have regained worldwide exclusive rights from Roche to research, develop, manufacture and commercialize the Compounds, the Products and the Companion Diagnostics in all fields of use.

Financial Operations Overview

As of December 31, 2022, we had cash, cash equivalents and marketable securities of $646.7 million. Net cash used in operating activities was $121.0 million for the year ended December 31, 2022.

We expect that our net cash used in operating activities will increase significantly as we advance our product candidates through preclinical and clinical development, seek regulatory approval, and prepare for and, if approved, proceed to commercialization; acquire, discover, validate and develop additional product candidates; obtain, maintain, protect and enforce our intellectual property portfolio; and hire additional personnel. In addition, we may incur additional costs as we continue to operate as a public company. We believe that our available cash and cash equivalents will be sufficient to fund our planned operations into 2026.

We do not have any products approved for sale and have not generated any product revenue since inception. We do not anticipate generating any revenue from product sales for the foreseeable future. Our ability to generate product revenue will depend on the successful development, regulatory approval and eventual commercialization of one or more of our product candidates. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through private or public equity or debt financings, collaborative or other arrangements with third parties, or through other sources of financing. Adequate funding may not be available to us on acceptable terms, or at all. If we fail to raise capital or enter into such agreements as and when needed, we may have to significantly delay, scale back or discontinue the development and commercialization of our product candidates.
We plan to continue to use third-party service providers, including CROs to carry out our preclinical and clinical development and CMOs to manufacture and supply the materials to be used during the development of our product candidates. Additionally, we expect to rely on CMOs for the manufacture of commercial supply of any product candidate we may successfully develop.

As we continue to advance our programs, we expect to incur significantly higher expenses over the next several years. We anticipate that our expenses will increase significantly in connection with our ongoing activities, as we:

- continue clinical development of bemnifosbuvir as a monotherapy for the treatment of COVID-19;
- advance the clinical development of the combination of bemnifosbuvir and ruzasvir for the treatment of HCV;
- continue discovery and IND-enabling activities in anticipation of nominating a protease inhibitor product candidate for the treatment of COVID-19;
- initiate clinical development of bemnifosbuvir in combination with a protease inhibitor for the treatment of COVID-19;
- manufacture increasing quantities of bemnifosbuvir drug substance and drug product in anticipation of potential commercialization;
- seek market approval and prepare for potential commercialization of product candidates we may successfully develop;
- acquire or in-license clinical stage drug candidates, form strategic alliances or establish collaborations with third parties;

- maintain, expand, protect and enforce our intellectual property portfolio;
- hire additional research, development and administrative personnel; and
- establish commercialization capabilities if we are successful in developing our product candidates.

Components of Results of Operations

Revenue

We do not have any products approved for sale and to date, we have not generated any revenue from product sales.

Our revenue has been collaboration revenue solely derived from the Roche License Agreement, which became effective in October 2020 and terminated on February 10, 2022. If our development efforts for our product candidates are successful and result in commercialization, we may generate additional revenue in the future from a combination of product sales or payments from collaboration or license agreements that we may enter into with third parties.

Operating Expenses

Research and Development Expenses

Substantially all of our research and development expenses consist of expenses incurred in connection with the development of our product candidates. These expenses include external costs consisting of fees paid to third parties, including CROs and CMOs, to conduct certain research and development activities on our behalf and consulting costs, as well as internal costs consisting of payroll and personnel-related expenses, including salaries and bonuses, employee benefit costs and stock-based compensation expenses for our research and product development employees and allocated overhead, including rent, equipment, depreciation, information technology costs and utilities attributable to our research and development personnel. We expense both internal and external research and development expenses as they are incurred. In circumstances where amounts have been paid in advance or in excess of costs incurred, we record a prepaid expense, which is expensed as services are performed or goods are delivered.

A significant portion of our research and development costs have been external costs, which we track by therapeutic area. We have not historically tracked our internal research and development expenses by therapeutic area as they are deployed across multiple programs.

As discussed in Note 3 to our consolidated financial statements, during the term of the Roche License Agreement which terminated in February 2022, we and Roche shared certain manufacturing and clinical development costs on a 50/50 basis. Billings to us by Roche for our percentage share of such expenses were recorded in research and development expenses. These costs represented a substantial portion of our research and development expenses and a material portion of our total expenses during the year ended December 31, 2021. During the year ended December 31, 2022, we recorded a net reduction to research and development expenses of $6.9 million related to credits received from Roche. These credits were the result, following the termination of the Roche License Agreement, of changes and adjustments [by Roche] in estimated amounts of expenses reported by Roche during the period in which we and Roche shared costs associated with the development of bemnifosbuvir.

The following table summarizes our external research and development expenses by indication and internal research and development expenses:

	Years Ended December 31,		
	2022	2021	2020
	(in thousands)		
COVID-19 external costs	$ 19,546	$ 93,508	$ 23,043
Dengue external costs	11,150	9,396	2,167
HCV external costs	5,817	27,514	1,831
RSV external costs	2,135	1,887	1,127
Internal research and development costs	43,288	34,900	9,855
Total research and development expenses	$ 81,936	$ 167,205	$ 38,023

We are focusing substantially all of our resources on the development of our product candidates, particularly bemnifosbuvir. We expect our research and development expenses to increase substantially for at least the next few years, as we seek to initiate additional clinical trials for our product candidates, complete our clinical programs, pursue regulatory approval of our product candidates and prepare for the possible commercialization of these product candidates. Predicting the timing or cost to complete our clinical programs or validation of our commercial manufacturing and supply processes is difficult and delays may occur because of many factors, including factors outside of our control. For example, if the FDA or other regulatory authorities were to require us to conduct clinical trials beyond those that we currently anticipate, we could be required to expend significant additional financial resources and time on the completion of clinical development. Furthermore, we are unable to predict when or if our product candidates will receive regulatory approval with any certainty.

General and Administrative Expenses

General and administrative expenses consist principally of payroll and personnel expenses, including salaries and bonuses, benefits and stock-based compensation expenses, professional fees for consulting, accounting and tax services, legal fees and expenses related to intellectual property and corporate matters, allocated overhead, including rent, equipment, depreciation, information technology costs and utilities attributable to our general and administrative personnel, and other general operating expenses not otherwise classified as research and development expenses.

We anticipate that our general and administrative expenses will continue to increase as a result of increased personnel costs, expanded infrastructure, increased compliance, consulting, legal and accounting services costs, and costs associated with support of increasing research and development activities, including more advanced clinical development of our product candidates and the initiation of activities in preparation for potential commercialization of any product candidates that we may successfully develop. Increasing costs associated with operating as a public company are also expected to result in the incurrence of additional general and administrative expenses.

Interest Income and Other, Net

Interest income and other, net, consists primarily of interest income earned on our cash, cash equivalents and marketable securities.

Income Taxes

Income taxes consists primarily of federal and state current income taxes.

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

The following table summarizes our results of operations for the periods indicated:

	Years Ended December 31,		
	2022	2021	Change
	(in thousands)		
Collaboration revenue	$ —	$ 351,367	$ (351,367)
Operating expenses:			
Research and development	81,936	167,205	(85,269)
General and administrative	48,714	45,785	2,929
Total operating expenses	130,650	212,990	(82,340)
Income (loss) from operations	(130,650)	138,377	(269,027)
Interest income and other, net	11,151	213	10,938
Income (loss) before income taxes	(119,499)	138,590	(258,089)
Income tax benefit (expense)	3,590	(17,400)	20,990
Net income (loss)	$ (115,909)	$ 121,190	$ (237,099)

Revenue

Collaboration revenue for the year ended December 31, 2021 was derived from the Roche License Agreement that was executed in October 2020 and terminated in February 2022. As discussed in Note 3 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, following receipt in November 2021 of the notice from Roche terminating the agreement, we recognized all remaining deferred revenue in 2021. We had no collaboration revenue for the year ended December 31, 2022.

Research and Development Expenses

Research and development expenses decreased by $85.3 million from $167.2 million for the year ended December 31, 2021 to $81.9 million for the year ended December 31, 2022. The decrease in research and development expenses was primarily due to a $93.7 million decrease in external expenses. This decrease principally resulted from the discontinuation in February 2022 of our obligation to share costs incurred by Roche in connection with Roche's development of bemnifosbuvir. This cost sharing obligation ended simultaneous with the termination of the Roche License Agreement. Associated with the Roche License Agreement, we recorded a net credit of $6.9 million for the year ended December 31, 2022 compared to expense of $76.6 million for the year ended December 31, 2021. In addition, we recorded a $25.0 million charge related to the one time upfront payment for the Merck license agreement during the year ended December 31, 2021. Partially offsetting the decrease was an increase of $8.4 million in internal costs primarily due to an increase in personnel-related expenses, including salaries and bonuses, benefits and stock-based compensation expense of $3.2 million for our research and product development employees and consulting fees, and $1.0 million in other research and development expenses.

General and Administrative Expenses

General and administrative expenses increased by $2.9 million from $45.8 million for the year ended December 31, 2021 to $48.7 million for the year ended December 31, 2022. The increase in general and administrative expenses was primarily due to the expansion of our organization and reflected an increase of $4.2 million in payroll and personnel-related expenses, including salaries, benefits and stock-based compensation expense of $3.3 million; partially offset by a decrease in professional fees of $1.2 million; and an increase in other general and administrative expenses of $0.6 million.

Interest Income and Other, Net

Interest income and other, net, increased by $10.9 million for the year ended December 31, 2022 compared to the year ended December 31, 2021, primarily due to investing in higher yield marketable securities and higher interest rates.

Income Taxes

We recorded a net benefit for income taxes of $3.6 million for the year ended December 31, 2022 compared to a provision for income taxes of $17.4 million for the year ended December 31, 2021. The net benefit recorded for the year ended December 31, 2022 was primarily the result of changes in estimates between our original provision for 2021 income taxes and the actual amounts reflected in the income tax returns as filed. For the year ended December 31, 2021, we recorded income tax expense related to pre-tax income earned primarily due to amounts received from the Roche License Agreement.

Comparison of the Years Ended December 31, 2021 and 2020

The following table summarizes our results of operations for the periods indicated:

	Years Ended December 31,		
	2021	2020	Change
	(in thousands)		
Collaboration revenue	$ 351,367	$ 48,633	$ 302,734
Operating expenses:			
Research and development	167,205	38,023	129,182
General and administrative	45,785	21,640	24,145
Total operating expenses	212,990	59,663	153,327
Loss from operations	138,377	(11,030)	149,407
Interest income and other, net	213	83	130
Income (loss) before income taxes	138,590	(10,947)	149,537
Income tax expense	(17,400)	—	(17,400)
Net income (loss)	$ 121,190	$ (10,947)	$ 132,137

Revenue

Collaboration revenue for the years ended December 31, 2021 and 2020 was derived from the Roche License Agreement that was executed in October 2020. See Note 3 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for a description of the accounting treatment of the Roche License Agreement, including recognition of all remaining deferred revenue following receipt of the termination notice from Roche.

Research and Development Expenses

Research and development expenses increased by $129.2 million from $38.0 million for the year ended December 31, 2020 to $167.2 million for the year ended December 31, 2021. The increase in research and development expenses was primarily due to a $104.1 million increase in external expenses incurred related to CRO and CMO services in connection with the advancement of product candidates for the treatment of COVID-19, HCV and dengue, including $76.6 million related to our share of costs incurred by Roche and a $25.0 million charge related to the upfront payment for the license agreement with Merck. In addition, there was an increase of $25.0 million in internal spend primarily due to an increase in personnel-related expenses, including salaries and bonuses, benefits and stock-based compensation expense of $14.6 million for our research and product development employees and consulting fees, and $2.4 million in other research and development expenses. Research and development expenses include a reduction of $7.3 million representing a reimbursement of Roche's share of certain expenses incurred that are subject to ASC 808 as discussed in Note 3 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

General and Administrative Expenses

General and administrative expenses increased by $24.1 million from $21.6 million for the year ended December 31, 2020 to $45.8 million for the year ended December 31, 2021. The increase in general and administrative expenses was primarily due to the expansion of our organization and reflected an increase of $20.6 million in payroll and personnel-related expenses, including salaries, benefits and stock-based

compensation expense of $17.6 million; an increase in professional fees of $2.6 million; and an increase in other general and administrative expenses of $0.9 million.

Interest Income and Other, Net

Interest income and other, net, increased by $0.1 million for the year ended December 31, 2021 compared to the year ended December 31, 2020, primarily due to higher balances of cash equivalents.

Income Taxes

Income taxes were $17.4 million and $0 million for the years ended December 31, 2021 and 2020, respectively. The effective tax rate for the years ended December 31, 2021 and 2020 was 12.5% and 0%, respectively. The increase in income tax expense was primarily due to revenue recognized in 2021 from our former collaboration with Roche.

Liquidity and Capital Resources

Sources of Liquidity

As of December 31, 2022, we had cash, cash equivalents and marketable securities of $646.7 million. We believe that our available cash, cash equivalents and marketable securities will be sufficient to fund our planned operations into 2026.

We entered into an open market sales agreement ("Sales Agreement"), with Jeffries, LLC ("Jeffries") in 2021 pursuant to which we may from time to time offer and sell shares of our common stock for an aggregate offering price of up to $200.0 million, through or to Jeffries, acting as sales agent or principal. We have agreed to pay Jeffries a commission of 3.0% of the aggregate gross proceeds from each sale of shares, reimburse legal fees and disbursements and provide Jeffries with customary indemnification and contribution rights. As of December 31, 2022, no shares have been issued under the Sales Agreement.

Future Funding Requirements

To date, we have not generated any product revenue. We do not expect to generate any product revenue unless and until we obtain regulatory approval of and commercialize any of our product candidates and we do not know when, or if, this will occur. We expect to continue to incur increased expenditures for the foreseeable future, and we expect our expenses to increase as we continue the development of, and seek regulatory approvals for, our product candidates and begin to commercialize any approved products. We are subject to all of the risks typically related to the development of new product candidates, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. Moreover, we expect to incur additional general and administrative costs as we continue to operate as a public company and expand our organization to support more advanced clinical development of our product candidates and the initiation of activities in preparation for potential commercialization of our product candidates.

We will continue to require additional capital to develop our product candidates and fund operations for the foreseeable future. We may seek to raise capital through public or private equity or debt financings, collaborative arrangements with third parties, or through other sources of financing. We anticipate that we may need to raise substantial additional capital, the requirements for which will depend on many factors, including:

- the scope, timing, rate of progress and costs of our drug discovery efforts, preclinical development activities, laboratory testing and clinical trials for our product candidates;
- the number and scope of clinical programs we decide to pursue;
- the cost, timing and outcome of preparing for and undergoing regulatory review of our product candidates;
- the scope and costs of development and commercial manufacturing activities;
- the cost and timing associated with commercializing our product candidates, if they receive marketing approval;
- the extent to which we acquire or in-license other product candidates and technologies;

- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- our efforts to enhance operational systems and our ability to attract, hire and retain qualified personnel, including personnel to support the development of our product candidates and, ultimately, the sale of our products, following regulatory approval;
- our implementation of operational, financial and management systems; and
- the costs associated with being a public company.

A change in the outcome of any of these or other variables with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of one or more of our product candidates. Furthermore, our operating plans may change in the future, and we will continue to require additional capital to meet operational needs and capital requirements associated with such operating plans. If we raise additional funds by issuing equity securities, our stockholders may experience dilution. Any future debt financing into which we enter may impose upon us additional covenants that restrict our operations, including limitations on our ability to incur liens or additional debt, pay dividends, repurchase our common stock, make certain investments or engage in certain merger, consolidation or asset sale transactions. Any debt financing or additional equity that we raise may contain terms that are not favorable to us or our stockholders.

Adequate funding may not be available to us on acceptable terms or at all. Our failure to raise capital as and when needed could have a negative impact on our financial condition and our ability to pursue our business strategies. If we are unable to raise additional funds when needed, we may be required to delay, reduce, or terminate some or all of our development programs and clinical trials or we may also be required to sell or license to others rights to our product candidates in certain territories or indications that we would prefer to develop and commercialize ourselves. If we are required to enter into collaborations and other arrangements to supplement our funds, we may have to give up certain rights that limit our ability to develop and commercialize our product candidates or may have other terms that are not favorable to us or our stockholders, which could materially affect our business and financial condition.

Market volatility, inflation, interest rate fluctuations and concerns related to the COVID-19 pandemic and geopolitical events, including civil or political unrest (such as the ongoing conflict between Ukraine and Russia), may have a significant impact on the availability of funding sources and the terms on which any funding may be available.

See Part I, Item 1A,“Risk Factors” for additional risks associated with our substantial capital requirements.

Summary Statement of Cash Flows

The following table sets forth the primary sources and uses of cash, cash equivalents, and restricted cash for each of the periods presented below:

	Years Ended December 31,		
	2022	2021	2020
	(in thousands)		
Net cash provided by (used in) operating activities	$ (120,982)	$ (87,005)	$ 296,734
Net cash used in investing activities	(455,410)	(4)	(26)
Net cash provided by financing activities	370	1,465	531,748
Net increase (decrease) in cash, cash equivalents and restricted cash	$ (576,022)	$ (85,544)	$ 828,456

Cash Flows from Operating Activities

Net cash used in operating activities for the year ended December 31, 2022 was $121.0 million. Cash used in operating activities was primarily due to net loss of $115.9 million, accretion of premium and discounts on marketable securities of $5.5 million, increase in prepaid expenses and other assets of $7.7

million and a decrease in accounts payable and accrued expenses of $39.6 million, partially offset by stock-based compensation of $46.7 million.

Net cash used in operating activities for the year ended December 31, 2021 was $87.0 million. Cash used in operating activities was primarily due to net income of $121.2 million increased by stock-based compensation of $39.6 million, an increase in accounts payable and accrued expenses of $54.2 million, an increase in prepaid expenses and other assets of $0.6 million all offset by a decrease in deferred revenue of $301.4 million.

Net cash provided by operating activities for the year ended December 31, 2020 was $296.7 million. Cash provided by operating activities was primarily due to an increase in deferred revenue of $301.4 million related to the Roche License Agreement, an increase in accounts payable and accrued expenses of $11.9 million and stock based compensation of $7.5 million, partly offset by the use of funds in our operations to develop our product candidates, resulting in a net loss of $10.9 million. Additional uses of cash during the period included an increase in prepaid expenses and other current assets $7.3 million and unbilled accounts receivable of $5.8 million. The net increase in deferred revenue of $301.4 was the result of the $350.0 million upfront payment offset by revenue recognized of $48.6 million.

Cash Flows from Investing Activities

Net cash used in investing activities for the year ended December 31, 2022 was $455.4 million and consisted of purchases of fixed assets of $1.9 million and purchases of marketable securities of $545.4 million, partially offset by sales and maturities of marketable securities of $91.9 million.

Net cash used in investing activities for each of the years ended December 31, 2021 and 2020 was less than $0.1 million and consisted of purchases of property and equipment.

Cash Flows from Financing Activities

Net cash provided by financing activities for the year ended December 31, 2022 was $0.4 million and consisted of proceeds from the exercise of stock options and proceeds from issuance of common stock under our Employee Stock Purchase Plan.

Net cash provided by financing activities for the year ended December 31, 2021 was $1.4 million and consisted of proceeds from issuance of common stock as a result of the exercise of stock options.
Net cash provided by financing activities for the year ended December 31, 2020 was $531.8 million, which consisted primarily of $106.6 million of net proceeds from the sale of Series D convertible preferred stock, $107.5 million of net proceeds from the sale of Series D-1 convertible preferred stock and $317.6 million of net proceeds from our IPO.

Contractual Obligations and Commitments

We lease our office space in Boston, Massachusetts under a non-cancelable operating sublease . The term of the sublease commenced on January 1, 2022 and will expire on December 31, 2026.

The following table summarizes our contractual obligations as of December 31, 2022:

	Payments Due by Period				
	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years	Total
	(in thousands)				
Operating lease obligations	$ 805	$ 1,659	$ 855	$ —	$ 3,319

We enter into contracts in the normal course of business with CROs for preclinical and clinical studies and testing, CMOs for manufacture and supply of our clinical trial materials and other third parties for other services and products used for operating purposes. These contracts do not contain any minimum purchase commitments and generally provide for termination following a certain period after notice, and therefore we believe that our non-cancelable obligations under these agreements are not material. Payments due upon cancelation consist only of payments for services provided and expenses incurred up to the date of cancelation.

In December 2021, we entered into a license agreement with Merck for the development, manufacture and commercialization of ruzasvir. Ruzasvir is the NS5A inhibitor we are developing in combination with bemnifosbuvir for the treatment of HCV.

Pursuant to the terms of the Merck License Agreement, we obtained from Merck an exclusive (subject to certain reserved rights to conduct internal research), sublicensable, and worldwide license under certain Merck patents and know-how to research, develop, manufacture, have manufactured, use, import, export, sell, offer for sale, and otherwise commercialize ruzasvir, or products containing ruzasvir for all therapeutic or prophylactic uses in humans.

In consideration for the rights we acquired under the Merck License Agreement, we paid Merck a non-refundable upfront payment in the amount of $25 million. We are obligated to pay Merck milestone payments of $135 million in the aggregate upon its achievement of certain development and regulatory milestones and up to $300 million in the aggregate upon its achievement of certain sales-based milestones. Additionally, we will pay Merck tiered royalties based on annual net sales of Products ranging from high single digits to mid-teens percentages. Our royalty payment obligations will continue until the later of (i) the expiration of the last to expire valid claim of a licensed Merck patent claiming such Product (or a Compound contained in such Product) and (ii) a period of years after the first commercial sale of such Product in such country. We may terminate the Merck License Agreement for convenience upon prior written notice. The first potential milestone would be payable upon the commencement of a Phase 3 clinical trial. The table above does not include the potential milestones or royalties that we may be obligated to pay under the Merck License Agreement.

The table above also does not include potential milestone and success fees that we may be required to pay under agreements we have entered into with certain consultants. We have an agreement with a consultant that requires payment of a success fee calculated as a percentage of certain product sales, subject to a cumulative maximum payout of $5.0 million. This success payment is contingent upon the occurrence of future events and the timing and likelihood of such payment is neither probable nor estimable.

Critical Accounting Policies and Estimates

Our financial statements have been prepared in accordance with US generally accepted accounting principles (“GAAP”). The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements and the reported expenses incurred during the reporting periods. Our estimates are based on our 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. The effects of material revisions in estimates, if any, will be reflected in the consolidated financial statements prospectively from the date of change in estimates.

Our critical accounting policies are those policies that require the most significant judgements and estimates in the preparation of the financial statements. Management has determined that our most critical accounting policies are those relating to revenue recognition, accrued research and development expenses and stock based compensation.

Revenue Recognition

As of December 31, 2022, all of our revenue to date had been collaboration revenue generated under the Roche License Agreement.

We analyze our collaboration arrangements to assess whether they are within the scope of Accounting Standards Codification ASC Topic 808, *Collaborative Arrangements (“*ASC 808”), to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards that are dependent on the commercial success of such activities. If we conclude that some or all aspects of the arrangement are within the scope of ASC 808 and do not represent a transaction with a customer, we recognize our allocation of the shared costs incurred with respect to the jointly conducted activities as a component of the related expense in the period incurred. If we conclude that some or all aspects of the arrangement represent a

transaction with a customer, we account for those aspects of the arrangement within the scope of ASC 606, *Revenue from Contracts with Customers* (“ASC 606”).

To determine the appropriate amount of revenue to be recognized for arrangements that we determine are within the scope of ASC 606, we perform the following steps: (i) identify the contract(s) with the customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) each performance obligation is satisfied. ASC 606 requires significant judgment and estimates and results in changes to, but not limited to: (i) the determination of the transaction price, including estimates of variable consideration, (ii) the allocation of the transaction price, including the determination of estimated selling price, and (iii) the pattern of recognition, including the application of proportional performance as a measure of progress on service-related promises and application of point-in-time recognition for supply-related promises.

The transaction price is generally comprised of an upfront payment due at contract inception and variable consideration in the form of payments for our services and materials and milestone payments due upon the achievement of specified events. Other payments we could be entitled to include tiered royalties earned when customers recognize net sales of licensed products. We consider the existence of any significant financing component within our arrangements and have determined that a significant financing component does not exist in our arrangements as substantive business purposes exist to support the payment structure other than to provide a significant benefit of financing. We measure the transaction price based on the amount of consideration to which we expect to be entitled in exchange for transferring the promised goods and/or services to the customer. We utilize either the expected value method or the most likely amount method to estimate the amount of variable consideration, depending on which method is expected to better predict the amount of consideration to which we will be entitled. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. With respect to arrangements that include payments for a development or regulatory milestone payment, we evaluate whether the associated event is considered probable of achievement and estimate the amount to be included in the transaction price using the most likely amount method. Milestone payments that are not within our control or the licensee, such as those dependent upon receipt of regulatory approval, are not considered to be probable of achievement until the triggering event occurs. At the end of each reporting period, we re-evaluate the probability of achievement of each milestone and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenue and net loss in the period of adjustment. For arrangements that include sales-based royalties, including milestone payments based upon the achievement of a certain level of product sales, wherein the license is deemed to be the sole or predominant item to which the payments relate, we recognize revenue upon the later of: (i) when the related sales occur or (ii) when the performance obligation to which some or all of the payment has been allocated has been satisfied (or partially satisfied). Consideration that would be received for optional goods and/or services is excluded from the transaction price at contract inception.

We generally allocate the transaction price to each performance obligation based on a relative standalone selling price basis. We develop assumptions that require judgment to determine the standalone selling price for each performance obligation in consideration of applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated research and development costs. However, in certain instances, we allocate variable consideration entirely to one or more performance obligation if the terms of the variable consideration relate to the satisfaction of the respective performance obligation and the amount allocated is consistent with the amount we would expect to receive for the satisfaction of the respective performance obligation.

We recognize revenue based on the amount of the transaction price that is allocated to each respective performance obligation when or as the performance obligation is satisfied by transferring a promised good or service to the customer. For performance obligations that are satisfied at a point in time, we recognize revenue when control of the goods and/or services is transferred to the customer. For performance obligations that are satisfied over time, we recognize revenue by measuring the progress toward complete satisfaction of the performance obligation using a single method of measuring progress

which depicts the performance in transferring control of the associated goods and/or services to the customer. We generally use input methods to measure the progress toward the complete satisfaction of performance obligations satisfied over time. With respect to arrangements containing a license to our intellectual property that is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenue from amounts allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. Significant management judgment is required in determining the level of effort and costs required under an arrangement and the period over which we are expected to complete our performance obligations under an arrangement. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenue and net loss in the period of adjustment.

Until receipt in November 2021 of the notice from Roche that Roche was terminating the Roche License Agreement effective February 2022, we recognized collaboration revenue over the expected performance period based on its measure of progress towards the completion of certain activities referred to as its Combined Performance Obligation. We concluded that the notice of termination represents a contract modification for accounting purposes. We further concluded that upon receipt of the notice of termination, the Combined Performance Obligation has been completely satisfied. As a result, we recognized all remaining deferred revenue as collaboration revenue within the consolidated statements of operations and comprehensive income for the year ended December 31, 2021 (see Note 3, Collaboration Revenue, for a detailed discussion).

Contract costs

We recognize as an asset the incremental costs of obtaining a contract with a customer if the costs are expected to be recovered. We have elected a practical expedient wherein we recognize the incremental costs of obtaining a contract as an expense when incurred if, at inception, the expected amortization period of the asset that we otherwise would have recognized is one year or less. In connection with the Roche License Agreement, we incurred an incremental cost of $7.0 million, which was included in general and administrative costs in the statement of operations and comprehensive loss for the year ended December 31, 2021 included elsewhere in this Annual Report on Form 10-K.

Accrued Research and Development

We have entered into various agreements with CMOs and CROs. Our research and development accruals are estimated based on the level of services performed, progress of the studies, including the phase or completion of events, and contracted costs. The estimated costs of research and development provided, but not yet invoiced, are included in accrued liabilities on the balance sheet. If the actual timing of the performance of services or the level of effort varies from the original estimates, we will adjust the accrual accordingly. Payments made to CMOs and CROs under these arrangements in advance of the performance of the related services are recorded as prepaid expenses and other current assets until the services are rendered. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Stock-Based Compensation

We use a fair value-based method to account for all stock-based compensation arrangements with employees and non-employees, including stock options and stock awards. The fair value of the option granted is recognized on a straight-line basis over the period during which an optionee is required to provide services in exchange for the option award, known as the requisite service period, which usually is the vesting period. In determining fair value of the stock options granted, we use the Black–Scholes model, which requires the input of subjective assumptions. These assumptions include: estimating the fair

market value of the common stock, estimating the length of time employees will retain their vested stock options before exercising them (expected term), the estimated volatility of our common stock price over the expected term (expected volatility), risk-free interest rate and expected dividends. See Note 10 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K for information concerning certain of the specific assumptions we used in applying the Black-Scholes option pricing model to determine the estimated fair value of our stock options granted during the years ended December 31, 2022, 2021 and 2020, respectively. Estimating the fair value of our common stock prior to the completion of our initial public offering involved significant judgement and the use of estimates.

Estimating the Fair Value of Common Stock

Prior to our IPO, we were required to estimate the fair value of the common stock underlying our share-based awards when performing the fair value calculations using the Black-Scholes option pricing model. Prior to our IPO, the fair value of the common stock underlying our stock options has been determined on each grant date by our board of directors, with input from management, considering the most recently available third-party valuation of our common shares. All options to purchase shares of our common stock are intended to be granted with an exercise price per share no less than the estimated fair value per share of our common stock underlying those options on the date of grant, based on the information known to us on the date of grant.

In the absence of a public trading market for our common stock prior to our IPO, on each grant date, we developed an estimate of the fair value of our common stock based on valuations from an independent third-party valuation firm using information known to us on the date of grant, a review of any recent events and their potential impact on the estimated fair value per share of the common stock.

The third-party valuations of our common stock were determined in accordance with the guidelines outlined in the American Institute of Certified Public Accountants Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation (“Practice Aid”).

The assumptions used to determine the estimated fair value of our common stock are based on numerous objective and subjective factors, combined with management judgment, including:

- external market conditions affecting the pharmaceutical and biotechnology industry and trends within the industry;
- our stage of development and business strategy;
- the rights, preferences and privileges of our redeemable convertible preferred stock relative to those of our common stock;
- the prices at which we sold shares of our redeemable convertible preferred stock;
- our financial condition and operating results, including our levels of available capital resources;
- the progress of our research and development efforts;
- equity market conditions affecting comparable public companies; and
- general US market conditions and the lack of marketability of our common stock.

The Practice Aid identifies various available methods for allocating enterprise value across classes and series of capital stock to determine the estimated fair value of common stock at each valuation date. In accordance with the Practice Aid, we considered the following methods:

- *Option Pricing Method*. Under the option pricing method, or OPM, shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The estimated fair values of the preferred and common stock are inferred by analyzing these options.
- *Probability-Weighted Expected Return Method.* The probability-weighted expected return method, or PWERM, is a scenario-based analysis that estimates value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class.

Based on our early stage of development and other relevant factors, we determined that OPM method as well as a hybrid approach of the OPM and the PWERM methods were the most appropriate methods for allocating our enterprise value to determine the estimated fair value of our common stock. In determining the estimated fair value of our common stock, our board of directors also considered the fact that our stockholders could not freely trade our common stock in the public markets. Accordingly, we applied discounts to reflect the lack of marketability of our common stock based on the weighted-average expected time to liquidity. The estimated fair value of our common stock at each grant date reflected a non-marketability discount partially based on the anticipated likelihood and timing of a future liquidity event.

Subsequent to the completion of our IPO, the fair value of our common stock is based on the daily closing quoted market price of our common stock.

We also account for any modifications to share based payments in accordance with ASC Topic 718, *Compensation – Stock Compensation* ("ASC 718").

Cash and Cash Equivalents

We consider all highly-liquid investments with an original maturity, or a remaining maturity at the time of purchase, of three months or less to be cash equivalents. Our cash equivalents include money market funds and commercial paper, which are highly liquid and have strong credit ratings. These investments are subject to minimal credit and market risks. Cash and cash equivalents are stated at cost, which approximates market value.

Marketable Securities

Our investment strategy is focused on capital preservation. We invest in instruments that meet the credit quality standards outlined in our investment policy. Marketable securities consist of investments with maturities greater than three months. Marketable securities include US treasury obligations, US agency obligations, corporate debt, commercial paper and asset-backed securities. We classify all of our marketable securities as available-for-sale. Accordingly, these investments are recorded at fair value. Unrealized gains and losses are recorded as a component of other comprehensive income within stockholders' equity. Amortization and accretion of discounts and premiums are recorded as interest income.

Fair Value Measurements

Fair value is defined as the price that would be received upon sale of an asset or paid to transfer a liability between market participants at measurement dates. ASC 820, *Fair Value Measurement,* establishes a three-level valuation hierarchy for instruments measured at fair value. The hierarchy is based on the transparency of inputs to the valuation of an asset or liability as of the measurement date. The three levels are defined as follows:
Level 1—Inputs to the valuation methodology are quoted prices (unadjusted) for identical assets or liabilities in active markets.
Level 2—Inputs to the valuation methodology include quoted prices for similar assets and liabilities in active markets, and inputs that are observable for the asset or liability, either directly or indirectly, for substantially the full term of the financial instrument.
Level 3—Inputs to the valuation methodology are unobservable and significant to the fair value measurement.

Concentration of Credit Risk and Off-balance Sheet Risk

Financial instruments that potentially subject us to concentrations of credit risk primarily consist of cash equivalents and marketable securities. Under our investment policy, we limit amounts invested in such securities by credit rating, maturity, industry group, investment type and issuer, except for securities issued by the US government. We do not believe that we are subject to any significant concentrations of credit risk from these financial instruments. We have no financial instruments with off-balance sheet risk, such as foreign exchange contracts, option contracts, or other foreign hedging arrangements.

Indemnification Agreements

We enter into standard indemnification arrangements in the ordinary course of business. Pursuant to these arrangements, we indemnify, hold harmless and agree to reimburse the indemnified parties for losses suffered or incurred by the indemnified party, including in connection with any trade secret, copyright, patent or other intellectual property infringement claim by any third party with respect to its technology. The term of these indemnification agreements is generally perpetual any time after the execution of the agreement. The maximum potential amount of future payments we could be required to make under these arrangements is not determinable. We have never incurred costs to defend lawsuits or settle claims related to these indemnification agreements. As a result, we believe the fair value of these agreements is minimal.

We have also agreed to indemnify our directors and officers for certain events or occurrences while the director or officer is, or was serving, at our request in such capacity. The indemnification period covers all pertinent events and occurrences during the director’s or officer’s service. The maximum potential amount of future payments we could be required to make under these indemnification agreements is not specified in the agreements; however, we have director and officer insurance coverage that reduces our exposure and enables us to recover a portion of any future amounts paid. We believe the estimated fair value of these indemnification agreements in excess of applicable insurance coverage is minimal.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Sensitivity

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates or exchange rates. As of December 31, 2022, we had cash, cash equivalents and marketable securities of $646.7 million, consisting of interest-bearing money market funds for which the fair value would be affected by changes in the general level of US interest rates. However, due to the short-term maturities and the low-risk profile of our cash equivalents, an immediate 10% relative change in interest rates would not have a material effect on the fair value of our cash equivalents or on our future interest income.

We do not believe that inflation, interest rate changes or foreign currency exchange rate fluctuations have had a significant impact on our results of operations for any periods presented herein.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of those financial statements is found in Item 15 of this Annual Report on Form 10-K.

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

None.

Item 9A. Controls and Procedures.

Management's Evaluation of our Disclosure Controls and Procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2022. Based upon such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2022, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control Over Financial Reporting

There were no changes to our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act.

Under the supervision of and with the participation of our principal executive officer and principal financial officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2022 based on the criteria set forth in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2022.

The effectiveness of our internal control over financial reporting as of December 31, 2022 has been audited by KPMG LLP, an independent registered public accounting firm, as stated in their report appearing below.

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Atea Pharmaceuticals, Inc.:

Opinion on Internal Control Over Financial Reporting

We have audited Atea Pharmaceuticals, Inc. and subsidiary's (the Company) internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive income (loss), convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the years in the three-year period ended December 31, 2022, and the related notes (collectively, the consolidated financial statements), and our report dated February 28, 2023 expressed an unqualified opinion on those consolidated 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 Annual 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 US federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included 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/ KPMG LLP

Boston, Massachusetts
February 28, 2023

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions That Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Code of Ethics

Our board of directors has adopted a written Code of Business Conduct and Ethics applicable to all officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer and controller, or persons performing similar functions. We have posted a current copy of our Code of Business Conduct and Ethics on our website at www.ateapharma.com in the "Investors" section under "Corporate Governance." We intend to satisfy the disclosure requirement under Item 5.05 of Form 8-K regarding amendment to, or waiver from, a provision of our Code of Business Conduct and Ethics, as well as Nasdaq's requirement to disclose waivers with respect to directors and executive officers, by posting such information on our website at the address and location specified above. The information contained on our website is not incorporated by reference into this Annual Report on Form 10-K.

Executive Officers and Directors

The information concerning our executive offers and directors required by this Item 10 is contained under the caption "Information About our Executive Officers and Directors" at the end of Part I, Item I, Business, of this Annual Report on Form 10-K. The remainder of the information required to be disclosed by this Item 10 will be included in our definitive Proxy Statement for the 2023 Annual Meeting of Stockholders under the headings "Corporate Governance," "Delinquent Section 16(a) Reports" (if applicable) and "Committees of the Board" and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 12 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 13 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services.

The information required by this Item 14 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Our independent registered public accounting firm is KPMG LLP, Boston, MA, Auditor Firm ID: 185.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(1) Financial Statements

The following documents are included on pages F-1 through F-26 attached hereto and are filed as part of this Annual Report on Form 10-K.

(2) Financial Statement Schedules

Schedules have been omitted since they are either not required or not applicable or the information is otherwise included herein.

(3) Exhibits

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed/ Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
3.1	Restated Certificate of Incorporation.	8-K	001-39661	3.1	11/5/2020	
3.2	Amended and Restated Bylaws.	8-K	001-39661	3.2	11/5/2020	
4.1	Specimen Stock Certificate evidencing the shares of common stock	S-1	333-249404	4.2	10/9/2020	
4.2	Description of Capital Stock	10-K	001-39661	4.2	3/30/2021	
4.3	Fourth Amended and Restated Stockholders Agreement, as amended	S-1/A	333-249404	4.1	10/23/2020	
10.1#	2020 Incentive Award Plan and form of agreements thereunder	S-1/A	333-249404	10.2	10/26/2020	
10.1-1#	Form of Performance-Based Restricted Stock Unit Award Agreement (CEO) under the 2020 Incentive Award Plan	10-K	001-39661	10.1.1	2/28/2022	
10.1-2#	Form of Performance-Based Restricted Stock Unit Award Agreement (Non-CEO Executive) under the 2020 Incentive Award Plan	10-K	001-39661	10.1.2	2/28/2022	
10.2#	2020 Employee Stock Purchase Plan	S-1/A	333-249404	10.3	10/26/2020	
10.3#	Non-Employee Director Compensation Program					*
10.4#	Form of Indemnification Agreement for Directors and Officers	S-1/A	333-249404	10.5	10/26/2020	
10.5^	License Agreement, dated as of December 23, 2021, by and between the Registrant and MSD International GMBH	10-K	001-39661	10.5	2/28/2022	
10.6#	Employment Agreement between the Company and Jean-Pierre Sommadossi, Ph.D., dated October 25, 2020	S-1/A	333-249404	10.9	10/26/2020	

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed/ Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
10.7#	Employment Agreement between the Company and Andrea Corcoran, dated October 25, 2020	S-1/A	333-249404	10.10	10/26/2020	
10.8#	Employment Agreement between the Company and Janet Hammond, MD, PhD, dated November 3, 2020	10-K	001-39661	10.8	3/30/2021	
10.9#	Employment Agreement between the Company and Arantxa Horga, MD, dated November 3, 2020	10-K	001-39661	10.9	3/30/2021	
10.10#	Employment Agreement between the Company and John Vavricka, dated November 3, 2020	10-K	001-39661	10.10	3/30/2021	
10.11#	Employment Agreement between the Company and Wayne Foster, dated November 3, 2020	10-K	001-39661	10.11	3/30/2021	
10.12#	2013 Stock Incentive Plan, as amended, and form of agreements thereunder	S-1	333-249404	10.1	10/9/2020	
10.13	Sublease Agreement, dated as of July 19, 2021, by and between the Company and DataRobot, Inc.	8-K	001-39661	10.1	7/23/2021	
10.13-1	Amendment to Sublease Agreement dated April 11, 2022 between the Company and DataRobot, Inc.	10-Q	001-39661	10.1	8/8/2022	
10.14#	Consulting Agreement, dated May 18, 2021, by and between the Company and Upstream Wellness and Health LLC.	8-K	001-39661	10.1	5/20/2021	
10.15	Consulting Agreement dated June 10, 2022, by and between the Company and Bruce Polsky, M.D.	10-Q	001-39661	10.2	8/8/2022	
21.1	List of Subsidiaries of the Registrant					*
23.1	Consent of Independent Registered Public Accounting Firm					*
31.1	Certification of Chief Executive Officer pursuant to Rule 13a-14(a)/15d-14(a).					*
31.2	Certification of Chief Financial Officer pursuant to Rule 13a-14(a)/15d-14(a).					*
32.1	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350.					**
32.2	Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350.					**
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					*

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed/ Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					*
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)					*

* Filed herewith.

** Furnished herewith.

^ Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

# Indicates management contract or compensatory plan.

Item 16. Form 10-K Summary

None.

SIGNATURES

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

ATEA PHARMACEUTICALS, INC.

Date: February 28, 2023

By: /s/ Jean-Pierre Sommadossi
Jean-Pierre Sommadossi, Ph.D.
President and Chief Executive Officer

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/ Jean-Pierre Sommadossi Jean-Pierre Sommadossi, Ph.D.	President, Chief Executive Officer and Chairman of the Board of Directors (principal executive officer)	February 28, 2023
/s/ Andrea Corcoran Andrea Corcoran	Chief Financial Officer and Executive Vice President, Legal and Secretary (principal financial officer)	February 28, 2023
/s/ Wayne Foster Wayne Foster	Executive Vice President, Chief Accounting Officer (principal accounting officer)	February 28, 2023
/s/ Franklin Berger Franklin Berger	Director (Lead Director)	February 28, 2023
/s/ Jerome Adams Jerome Adams, M.D., M.P.H	Director	February 28, 2023
/s/ Barbara Duncan Barbara Duncan	Director	February 28, 2023
/s/ Bruno Lucidi Bruno Lucidi	Director	February 28, 2023
/s/ Polly A. Murphy Polly A. Murphy, D.V.M., Ph.D.	Director	February 28, 2023
/s/ Bruce Polsky Bruce Polsky, M.D.	Director	February 28, 2023

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Atea Pharmaceuticals, Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Atea Pharmaceuticals, Inc. and subsidiary (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive income (loss), convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the years in the three-year period ended December 31, 2022, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

We also have 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, 2022, 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, 2023 expressed an unqualified opinion on the effectiveness of the Company's internal control over financial reporting.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated 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 consolidated 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 consolidated 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 consolidated 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 consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

Critical audit matters are matters arising from the current period audit of the consolidated financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. We determined that there are no critical audit matters.

/s/ KPMG LLP

We have served as the Company's auditor since 2014.

Boston, Massachusetts
February 28, 2023

ATEA PHARMACEUTICALS, INC.
Consolidated Balance Sheets
(in thousands, except share and per share amounts)

	December 31,	
	2022	**2021**
Assets		
Current assets		
Cash and cash equivalents	$ 188,460	$ 764,375
Marketable securities	458,249	—
Prepaid expenses and other current assets	14,213	8,028
Total current assets	660,922	772,403
Property and equipment, net	1,705	23
Restricted cash	198	305
Other assets	1,494	—
Operating lease right-of-use assets, net	2,389	161
Total assets	$ 666,708	$ 772,892
Liabilities and Stockholders' Equity		
Current liabilities		
Accounts payable	$ 2,551	$ 4,534
Accrued expenses and other current liabilities	15,206	52,152
Current portion of operating lease liabilities	721	197
Total current liabilities	18,478	56,883
Operating lease liabilities	2,403	—
Income taxes payable	5,255	5,932
Total liabilities	26,136	62,815
Commitments and contingencies (see Note 8)		
Stockholders' equity:		
Preferred stock, $0.001 par value per share; 10,000,000 shares authorized; no shares issued and outstanding as of December 31, 2022 and 2021	—	—
Common stock, $0.001 par value; 300,000,000 shares authorized; 83,287,639 and 83,102,730 shares issued and outstanding as of December 31, 2022 and 2021	83	83
Additional paid-in capital	701,052	653,964
Accumulated other comprehensive loss	(684)	—
Retained earnings (accumulated deficit)	(59,879)	56,030
Total stockholders' equity	640,572	710,077
Total liabilities and stockholders' equity	$ 666,708	$ 772,892

The accompanying notes are an integral part of these consolidated financial statements.

ATEA PHARMACEUTICALS, INC.
Consolidated Statements of Operations and Comprehensive Income (Loss)

(in thousands, except share and per share amounts)

	Years Ended December 31,		
	2022	**2021**	**2020**
Collaboration revenue	$ —	$ 351,367	$ 48,633
Operating expenses			
Research and development	81,936	167,205	38,023
General and administrative	48,714	45,785	21,640
Total operating expenses	130,650	212,990	59,663
Income (loss) from operations	(130,650)	138,377	(11,030)
Interest income and other, net	11,151	213	83
Income (loss) before income taxes	(119,499)	138,590	(10,947)
Income tax benefit (expense)	3,590	(17,400)	—
Net income (loss)	$ (115,909)	$ 121,190	$ (10,947)
Other comprehensive income (loss)			
Unrealized loss on available-for-sale investments	(684)	—	—
Comprehensive income (loss)	$ (116,593)	$ 121,190	$ (10,947)
Net income (loss) per share attributable to common stockholders			
Basic	$ (1.39)	$ 1.46	$ (0.51)
Diluted	$ (1.39)	$ 1.37	$ (0.51)
Weighted-average number of common shares used in computing net income (loss) per share attributable to common stockholders			
Basic	83,245,385	82,820,037	21,592,441
Diluted	83,245,385	88,249,243	21,592,441

The accompanying notes are an integral part of these consolidated financial statements.

ATEA PHARMACEUTICALS, INC.

Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)

(in thousands, except share amounts)

	Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated	Retained Earnings (Accumulated	Total Stockholders'
	Shares	Amount	Shares	Amount	Capital	OCI	Deficit)	Equity
Balance – January 1, 2020	33,645,447	$ 69,114	10,091,100	$ 10	$ 4,632	$ —	$ (54,213)	$ (49,571)
Issuance of Series D convertible preferred stock, net of issuance costs of $869	15,313,382	106,631	—	—	—	—	—	—
Issuance of Series D-1 convertible preferred stock, net of issuance costs of $15	8,973,261	107,485	—	—	—	—	—	—
Issuance of common stock for exercise of stock options	—	—	18,747	—	27	—	—	27
Stock-based compensation in connection with vesting of restricted stock	—	—	20,000	—	657	—	—	657
Initial public offering, net of issuance costs of $3,245	—	—	14,375,000	14	317,591	—	—	317,605
Conversion of preferred stock into common stock	(57,932,090)	(283,230)	57,932,090	58	283,172	—	—	283,230
Stock-based compensation expense	—	—	—	—	6,800	—	—	6,800
Net loss	—	—	—	—	—	—	(10,947)	(10,947)
Balance – December 31, 2020	—	—	82,436,937	82	612,879	—	(65,160)	547,801
Issuance of common stock for exercise of stock options	—	—	665,793	1	1,464	—	—	1,465
Stock-based compensation expense	—	—	—	—	39,621	—	—	39,621
Net income	—	—	—	—	—	—	121,190	121,190
Balance – December 31, 2021	—	—	83,102,730	83	653,964	—	56,030	710,077
Issuance of common stock for exercise of stock options	—	—	155,873	—	230	—	—	230
Issuance of common stock under ESPP			29,036		140			140
Stock-based compensation expense	—	—	—	—	46,718	—	—	46,718
Other comprehensive loss	—	—	—	—	—	(684)	—	(684)
Net loss	—	—	—	—	—	—	(115,909)	(115,909)
Balance – December 31, 2022	—	$ —	83,287,639	$ 83	$ 701,052	$ (684)	$ (59,879)	$ 640,572

The accompanying notes are an integral part of these consolidated financial statements.

ATEA PHARMACEUTICALS, INC.
Consolidated Statements of Cash Flows

(in thousands)

	Year Ended December 31,		
	2022	**2021**	**2020**
Cash flows from operating activities			
Net income (loss)	$ (115,909)	$ 121,190	$ (10,947)
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities			
Stock-based compensation expense	46,718	39,621	7,457
Depreciation and amortization expense	260	29	19
Accretion of premium and discounts on marketable securities	(5,465)	—	—
Changes in operating assets and liabilities			
Unbilled accounts receivable	—	—	(5,815)
Prepaid expenses and other current assets	(6,251)	(483)	(7,296)
Other assets	(1,494)	(161)	—
Accounts payable	(1,983)	10,289	(488)
Accrued expenses and other liabilities	(37,623)	43,877	12,437
Deferred revenue	—	(301,367)	301,367
Operating lease liabilities	765	—	—
Net cash provided by (used in) operating activities	(120,982)	(87,005)	296,734
Cash flows from investing activities			
Additions to property and equipment	(1,943)	(4)	(26)
Purchases of marketable securities	(545,352)	—	—
Sales and maturities of marketable securities	91,885	—	—
Net cash used in investing activities	(455,410)	(4)	(26)
Cash flows from financing activities			
Net proceeds from issuance of convertible preferred stock	—	—	214,116
Proceeds from issuance of common stock for exercise of stock options	230	1,465	27
Proceeds from issuance of common stock under ESPP	140	—	—
Net proceeds from initial public offering of common stock	—	—	317,605
Net cash provided by financing activities	370	1,465	531,748
Net increase (decrease) in cash, cash equivalents and restricted cash	(576,022)	(85,544)	828,456
Cash, cash equivalents and restricted cash at the beginning of period	764,680	850,224	21,768
Cash, cash equivalents and restricted cash at the end of period	$ 188,658	$ 764,680	$ 850,224
Cash, cash equivalents and restricted cash at the end of period			
Cash and cash equivalents	$ 188,460	$ 764,375	$ 850,117
Restricted cash	198	305	107
Total cash, cash equivalents and restricted cash	$ 188,658	$ 764,680	$ 850,224
Supplemental disclosure of non-cash financing activities			
Conversion of preferred stock to common stock upon closing of initial public offering	$ —	$ —	$ 283,230
Right of use assets obtained in exchange for operating lease liabilities	$ 2,938	$ —	$ —

The accompanying notes are an integral part of these consolidated financial statements.

ATEA PHARMACEUTICALS, INC.
Notes to Consolidated Financial Statements
(in thousands, except share and per share amounts)

1. Nature of Business

Atea Pharmaceuticals, Inc., together with its subsidiary Atea Pharmaceuticals Securities Corporation, is referred to on a consolidated basis as the "Company".

The Company is a clinical-stage biopharmaceutical company focused on discovering, developing and commercializing antiviral therapeutics to improve the lives of patients suffering from life-threatening viral infections.

In October 2020, the Company entered into a license agreement, ("Roche License Agreement") with F. Hoffmann-La Roche Ltd and Genentech, Inc. (collectively "Roche"), granting Roche an exclusive license to develop and commercialize certain of the Company's compounds including its lead product candidate bemnifosbuvir outside of the United States.

As part of the consideration, Roche agreed to pay the Company an upfront payment of $350,000 ("Roche Upfront Payment"), which was received in November 2020. In 2021, the Company also received $50,000 pursuant to a milestone under the Roche License Agreement.

On November 12, 2021, Roche provided the Company a notice of termination of the Roche License Agreement. Under the terms of the Roche License Agreement, the termination was effective in February 2022. Upon termination, the rights and licenses granted by the Company to Roche under the Roche License Agreement were returned to the Company, and the Company has full rights to continue the clinical development and future commercialization of bemnifosbuvir worldwide.

On November 3, 2020, the Company completed an initial public offering of its common stock ("IPO"). In connection with the IPO, the Company issued 14,375,000 shares of its common stock at $24.00 per share for net proceeds of $317,605 after deducting underwriting discounts and commissions and offering expenses payable by the Company. Upon closing of the IPO, all outstanding shares of the Company's convertible preferred stock converted into 57,932,090 shares of common stock.

The Company is subject to risks and uncertainties common to clinical-stage biopharmaceutical companies. These risks include, but are not limited to, potential failure of preclinical and clinical studies, uncertainties associated with research and development activities generally, competition from technical innovations of others, dependence upon key personnel, compliance with governmental regulations, the need to obtain marketing approval for any product candidate that the Company may develop, the need to gain broad acceptance among patients, payers and health care providers to successfully commercialize any product for which marketing approval is obtained and the need to secure and maintain adequate intellectual property protection for the Company's proprietary technology and products. Further, the Company is currently dependent on third-party service providers for much of its preclinical research, clinical development and manufacturing activities. Product candidates currently under development will require significant amounts of additional capital, and additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval, prior to commercialization. Even if the Company is able to generate revenues from the sale of its product candidates, if approved, it may not become profitable. If the Company fails to become profitable or is unable to sustain profitability on a continuing basis, then it may be unable to continue its operations at planned levels and be forced to reduce its operations.

The Company may seek additional capital through one or more of a combination of financing through the sale of additional equity securities, debt financing, or funding in connection with any new collaborative relationships it may enter into or other arrangements. There can be no assurance that the Company will be able to obtain such additional funding, on terms acceptable to the Company, on a timely basis or at all. The terms of any financing may adversely affect the holdings or the rights of the Company's existing stockholders. The Company believes that its cash and cash equivalents and marketable securities of $646,709 as of December 31, 2022 will be sufficient to fund its operations as currently planned through at least twelve months from the issuance of this Annual Report on Form 10-K.

In November 2021, the Company entered into an open market sales agreement ("Sales Agreement") with Jeffries LLC ("Jeffries"), under which the Company may from time to time offer and sell shares of its common stock for an aggregate offering price of up to $200.0 million, through or to Jeffries, acting as sales agent or principal. The shares will be offered and sold under the Company's shelf registration statement on Form S-3 and a related prospectus filed with the Securities and Exchange Commission ("SEC") on November 24, 2021, as amended. The Company has agreed to pay Jeffries a commission of 3.0% of the aggregate gross proceeds from each sale of shares, reimburse legal fees and disbursements and provide Jeffries with customary indemnification and contribution rights. As of December 31, 2022, no shares have been issued under the Sales Agreement.

The Company is also subject to risks associated with the COVID-19 global pandemic, including actual and potential delays associated with certain of its ongoing and anticipated trials, and potential negative impacts on the Company's business operations and its ability to raise additional capital to finance its operations. Geopolitical events, including civil or political unrest (such as the ongoing war between Ukraine and Russia), have resulted in a significant disruption of global business and financial markets. In addition, recent or future market volatility, increased inflation and higher interest rates, if sustained, may increase our cost of financing and may restrict our access to potential sources of future liquidity.

2. Summary of Significant Accounting Policies

Basis of Presentation and Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and in these accompanying notes. The Company bases its estimates on historical experience, known trends and other market-specific or other relevant factors and assumptions that it believes to be reasonable under the circumstances. On an ongoing basis, management evaluates its estimates, which include but are not limited to estimates of accrued research and development expenses, valuation of marketable securities, the valuation of stock-based awards, valuation of operating lease right-of-use assets and lease liabilities and income taxes. Changes in estimates are recorded in the period in which they become known.

Principles of Consolidation

The consolidated financial statements include the accounts of Atea Pharmaceuticals, Inc. and its wholly-owned subsidiary, Atea Pharmaceuticals Securities Corporation. All intercompany amounts have been eliminated in consolidation.

Reclassification

Certain items in the prior year's financial statements have been reclassified to conform to the current presentation.

Revenue Recognition

Through December 31, 2021, all of the Company's revenue was collaboration revenue generated from the Roche License Agreement.

Until receipt in November 2021 of the notice from Roche that Roche was terminating the Roche License Agreement effective February 2022, the Company recognized collaboration revenue over the expected performance period based on its measure of progress towards the completion of certain activities referred to as its Combined Performance Obligation. The Company concluded that the notice of termination represents a contract modification for accounting purposes. The Company further concluded that upon receipt of the notice of termination, the Combined Performance Obligation has been completely satisfied. As a result, the Company recognized all remaining deferred revenue as collaboration revenue within the consolidated statements of operations and comprehensive income for the year ended December 31, 2021 (see Note 3, Collaboration Revenue, for a detailed discussion).

The Company analyzes its collaboration arrangements to assess whether they are within the scope of Accounting Standards Codification ASC Topic 808, *Collaborative Arrangements ("*ASC 808"), to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards that are dependent on the commercial success of such activities. If the Company concludes that some or all aspects of the

arrangement are within the scope of ASC 808 and do not represent a transaction with a customer, the Company recognizes its allocation of the shared costs incurred with respect to the jointly conducted activities pursuant to ASC 730, *Research and Development*. As such, the Company will expense costs as incurred, including any reimbursements made, and recognize reimbursements received as a reduction of research and development expense. If the Company concludes that some or all aspects of the arrangement represent a transaction with a customer, the Company accounts for those aspects of the arrangement within the scope of ASC 606, *Revenue from Contracts with Customers* ("ASC 606").

To determine the appropriate amount of revenue to be recognized for arrangements that the Company determines are within the scope of ASC 606, it performs the following steps: (i) identify the contract(s) with the customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) each performance obligation is satisfied. ASC 606 requires significant judgment and estimates and results in changes to, but not limited to: (i) the determination of the transaction price, including estimates of variable consideration, (ii) the allocation of the transaction price, including the determination of estimated selling price, and (iii) the pattern of recognition, including the application of proportional performance as a measure of progress on service-related promises and application of point-in-time recognition for supply-related promises.

The transaction price is generally comprised of an upfront payment due at contract inception and variable consideration in the form of payments for the Company's services and materials and milestone payments due upon the achievement of specified events. Other payments the Company could be entitled to include tiered royalties earned when customers recognize net sales of licensed products. The Company considers the existence of any significant financing component within its arrangements and has determined that a significant financing component does not exist in its arrangements as substantive business purposes exist to support the payment structure other than to provide a significant benefit of financing. The Company measures the transaction price based on the amount of consideration to which it expects to be entitled in exchange for transferring the promised goods and/or services to the customer. The Company utilizes either the expected value method or the most likely amount method to estimate the amount of variable consideration, depending on which method is expected to better predict the amount of consideration to which the Company will be entitled. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. With respect to arrangements that include payments for a development or regulatory milestone payment, the Company evaluates whether the associated event is considered probable of achievement and estimate the amount to be included in the transaction price using the most likely amount method. Milestone payments that are not within the Company's control or the customer's, such as those dependent upon receipt of regulatory approval, are not considered to be probable of achievement until the triggering event occurs. At the end of each reporting period, the Company re-evaluates the probability of achievement of each milestone and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenue and net loss in the period of adjustment. For arrangements that include sales-based royalties, including milestone payments based upon the achievement of a certain level of product sales, wherein the license is deemed to be the sole or predominant item to which the payments relate, the Company recognizes revenue upon the later of: (i) when the related sales occur or (ii) when the performance obligation to which some or all of the payment has been allocated has been satisfied (or partially satisfied). Consideration that would be received for optional goods and/or services is excluded from the transaction price at contract inception.

The Company generally allocates the transaction price to each performance obligation based on a relative standalone selling price basis. The Company develops assumptions that require judgment to determine the standalone selling price for each performance obligation in consideration of applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated research and development costs. However, in certain instances, the Company allocates variable consideration entirely to one or more performance obligation if the terms of the variable consideration relate to the satisfaction of the respective performance obligation and the amount allocated is consistent with the amount the Company would expect to receive for the satisfaction of the respective performance obligation.

The Company recognizes revenue based on the amount of the transaction price that is allocated to each respective performance obligation when or as the performance obligation is satisfied by transferring a promised good or service to the customer. For performance obligations that are satisfied at a point in time, the Company recognizes revenue when control of the goods and/or services is transferred to the customer. For performance obligations that are satisfied over time, the Company recognizes revenue by measuring the progress toward complete satisfaction of the performance obligation using a single method of measuring progress which depicts the performance in transferring control of the associated goods and/or services to the customer. The Company generally uses input methods to measure the progress toward the complete satisfaction of performance obligations satisfied over time. With respect to arrangements containing a license to its intellectual property that is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue from amounts allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. Significant management judgment is required in determining the level of effort required under an arrangement and the period over which the Company is expected to complete its performance obligations under an arrangement. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenue and net loss in the period of adjustment.

Contract costs

The Company recognizes as an asset the incremental costs of obtaining a contract with a customer if the costs are expected to be recovered. The Company has elected the practical expedient in ASC 340, *Other Assets and Deferred Costs*, wherein it recognizes the incremental costs of obtaining a contract as an expense when incurred if, at inception, the expected amortization period of the asset that the Company otherwise would have recognized is one year or less. In connection with the Roche License Agreement, the Company incurred an incremental cost of $7,000, which was included in general and administrative costs in the accompanying statement of operations and comprehensive income(loss) for the year ended December 31, 2020.

Cash and Cash Equivalents

The Company considers all highly-liquid investments with an original maturity, or a remaining maturity at the time of purchase, of three months or less to be cash equivalents. The Company's cash equivalents include money market funds and commercial paper, which are highly liquid and have strong credit ratings. These investments are subject to minimal credit and market risks. Cash and cash equivalents are stated at cost, which approximates market value.

Marketable Securities

The Company's investment strategy is focused on capital preservation. The Company invests in instruments that meet the credit quality standards outlined in the Company's investment policy. Marketable securities consist of investments with maturities greater than three months. Investments not classified as cash equivalents with maturities of less than twelve months are classified as current assets on the consolidated balance sheet. Investments with maturities greater than twelve months for which the Company has the intent and ability to hold the investment for greater than twelve months are classified as

non-current on the consolidated balance sheet. Marketable securities include U.S. treasury obligations, U.S. agency obligations, corporate debt, commercial paper and asset-backed securities. The Company classifies all of its marketable securities as available-for-sale. Accordingly, these investments are recorded at fair value. Unrealized gains and losses are recorded as a component of other comprehensive income within stockholders' equity. Interest, dividends and amortization and accretion of discounts and premiums are recorded as interest income and other, net. The Company periodically reviews its marketable securities for impairment and adjusts these investments to their fair value when a decline in market value is deemed to be other than temporary. Declines in fair value judged to be other than temporary on marketable securities, if any, are included in interest income and other, net.

Concentrations of Credit Risk and Significant Suppliers

Financial instruments that potentially subject the Company to concentrations of credit risk primarily consist of cash equivalents and marketable securities. Under its investment policy, the Company limits amounts invested in such securities by credit rating, maturity, industry group, investment type and issuer, except for securities issued by the U.S. government. The Company does not believe that it is subject to any significant concentrations of credit risk from these financial instruments. The Company has no financial instruments with off-balance sheet risk, such as foreign exchange contracts, option contracts, or other foreign hedging arrangements.

The Company is dependent on third-party manufacturers to supply products for research and development activities in its programs. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements for the active pharmaceutical ingredients and formulated drugs related to these programs. These programs could be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients and formulated drugs.

Fair Value Measurements

Fair value is defined as the price that would be received upon sale of an asset or paid to transfer a liability between market participants at measurement dates. ASC 820, *Fair Value Measurement,* establishes a three-level valuation hierarchy for instruments measured at fair value. The hierarchy is based on the transparency of inputs to the valuation of an asset or liability as of the measurement date. The three levels are defined as follows:
Level 1—Inputs to the valuation methodology are quoted prices (unadjusted) for identical assets or liabilities in active markets.
Level 2—Inputs to the valuation methodology include quoted prices for similar assets and liabilities in active markets, and inputs that are observable for the asset or liability, either directly or indirectly, for substantially the full term of the financial instrument.
Level 3—Inputs to the valuation methodology are unobservable and significant to the fair value measurement of the assets and liabilities. The carrying amounts of accounts. payable, accrued and prepaid expenses and other current assets approximate their fair value due to short-term maturities.

Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation and amortization. Property and equipment are depreciated using the straight-line method over the estimated useful lives of the asset. The Company estimates the useful life of its assets as follows:

Asset	Estimated useful life
Laboratory equipment	Five years
Office furniture and fixtures	Five years
Computer hardware	Two years
Leasehold improvements	Shorter of useful life or remaining lease term

Maintenance and repairs that do not improve or extend the life of the respective asset are expensed to operations as incurred. Upon disposal of an asset, the related cost and accumulated depreciation are removed from the accounts and any resulting gain or loss is included in the consolidated statements of operations.

Other Assets

Other assets consist of a vendor deposit of $1,494 related to research and development activities.

Impairment of Long-lived Assets

The Company reviews long-lived assets when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparing the book value of the assets to the estimated undiscounted future net cash flows that the asset is expected to generate. If the estimated undiscounted future net cash flows are less than the book value, the asset is impaired, and the impairment loss to be recognized in income is measured as the amount by which the book value of the asset exceeds its fair value, which is measured based on the estimated discounted future net cash flows that the asset is expected to generate. No impairment losses were recorded during the years ended December 31, 2022, 2021 and 2020.

Leases

The Company accounts for leases in accordance with ASC Topic 842, *Lease Accounting*. At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease. Leases with a term greater than one year are recognized on the consolidated balance sheet as a right-of-use ("ROU") asset and current and non-current lease liabilities, as applicable. Operating lease liabilities and their corresponding ROU assets are recorded based on the present value of future lease payments over the expected remaining lease term. Lease cost for operating leases is recognized on a straight-line basis over the lease term as an operating expense. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses consist principally of costs associated with outsourced research and development activities, including preclinical and clinical development, manufacturing and research conducted by contract research organizations and academic institutions, employee compensation, including stock-based compensation and consulting expenses together with related expenses, professional fees and facility and overhead costs. Facility and overhead costs primarily include the allocation of rent, utility and office-related expenses attributable to research and development personnel. In circumstances where amounts have been paid in advance or in excess of costs incurred, the Company records a prepaid expense, which is expensed as services are performed or goods are delivered.

The Company has entered into various research and development contracts with third parties. These agreements are generally cancelable, and related payments are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies, including the phase of completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates.

Patent Costs

Costs to secure and maintain the Company's patents are expensed as incurred and are classified as general and administrative expenses in the Company's consolidated statements of operations.

Stock-based Compensation

Stock-based compensation expense is classified in the consolidated statement of operations and comprehensive income (loss) in the same manner in which the award recipient's payroll costs or service payments are classified. Stock-based awards granted to employees and non-employees are measured based on the estimated fair value of the awards using the Black-Scholes option pricing model ("Black-Scholes"). Stock-based compensation expense with respect to awards with service conditions is recognized using the straight-line method over the service period. Stock-based compensation with

respect to awards with performance conditions is recognized when satisfaction of the performance conditions is probable. Stock-based compensation is based on awards ultimately expected to vest and, as such, it is reduced by forfeitures. The Company accounts for forfeitures as they occur.

Black-Scholes requires the use of subjective assumptions which determine the fair value of stock-based awards. These assumptions include:

Fair value of common stock

Prior to the IPO, because there was no public market for the Company's common stock, the fair value of the Company's common stock underlying stock-based awards was estimated on each grant date by the board of directors. The Company developed an estimate on each grant date of the fair value of its common stock based on valuations from an independent third-party valuation firm using information known to the Company on the date of grant and a review of any recent events and their potential impact on the estimated fair value per share of the common stock. The third-party valuations of the Company's common stock were determined in accordance with the guidelines outlined in the American Institute of Certified Public Accountants Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation, or the Practice Aid. The assumptions used to determine the estimated fair value of the Company's common stock were based on numerous objective and subjective factors, combined with management judgment, including:

- external market conditions affecting the pharmaceutical and biotechnology industry and trends within the industry;
- the Company's stage of development and business strategy;
- the rights, preferences and privileges of the Company's then-outstanding redeemable convertible preferred stock relative to those of its common stock;
- the prices at which the Company sold shares of its then-outstanding redeemable convertible preferred stock;
- the Company's financial condition and operating results, including its levels of available capital resources;
- the progress of the Company's research and development efforts;
- equity market conditions affecting comparable public companies; and
- general U.S. market conditions and the lack of marketability at the time of the Company's common stock.

The Practice Aid identifies various available methods for allocating enterprise value across classes and series of capital stock to determine the estimated fair value of common stock at each valuation date. In accordance with the Practice Aid, the Company considered the following methods:

- *Option Pricing Method*. Under the option pricing method ("OPM"), shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The estimated fair values of the then-outstanding preferred stock and common stock were inferred by analyzing these options.
- *Probability-Weighted Expected Return Method.* The probability-weighted expected return method ("PWERM"), is a scenario-based analysis that estimates value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to the Company, as well as the economic and control rights of each share class.

Based on the Company's early stage of development and other relevant factors, the Company determined that OPM method as well as a hybrid approach of the OPM and the PWERM methods were the most appropriate methods for allocating its enterprise value to determine the estimated fair value of its common stock. In determining the estimated fair value of the Company's common stock, its board of directors also considered the fact that its stockholders could not freely trade its common stock in the public markets. Accordingly, the Company applied discounts to reflect the lack of marketability of its common stock based on the weighted-average expected time to liquidity. The estimated fair value of the

Company's common stock at each grant date reflected a non-marketability discount partially based on the anticipated likelihood and timing of a future liquidity event.

Upon the completion of the Company's initial public offering, the fair value of its common stock is based on the daily closing quoted market price of its common stock.

Risk-free interest rate—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of a stock-based award.

Expected term—The expected term represents the period that stock-based awards are expected to be outstanding. Given the Company's lack of specific history, the expected term for option grants is determined using the simplified method. The simplified method deems the term to be the average of the time-to-vesting and the contractual life of the stock-based awards.

Expected volatility—Since the Company was privately held through October 29, 2020 and did not have any trading history for its common stock, the expected volatility was estimated based on the average volatility for comparable publicly traded biotechnology companies over a period equal to the expected term of the stock-based awards. The comparable companies were chosen based on their similar size, stage in the life cycle or area of specialty. During the fiscal year ended December 31, 2022 the Company began to incorporate the historical volatility of its own stock price in its calculation of its expected volatility.

Expected dividend yield —The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

The Company also accounts for any modifications to share based payments in accordance with ASC Topic 718, *Compensation – Stock Compensation* (ASC 718).

The purchase price of the Company's common stock under the Company's 2020 Employee Stock Purchase Plan ("ESPP") is equal to 85% of the lesser of (i) the fair market value per share of its common stock on the first business day of an offering period and (ii) the fair market value per share of its common stock on the purchase date. The fair value of the discounted purchases made under ESPP is calculated using the Black-Scholes valuation model. The fair value of the look-back provision plus the 15% discount is recognized as compensation expense over the 180-day purchase period.

Income Taxes

The Company uses the asset and liability method of accounting for income taxes. Deferred tax assets and liabilities are recognized for the estimated future tax consequences attributable to temporary differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax base. Deferred tax assets are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. Deferred tax expense or benefit is the result of changes in the deferred tax assets and liabilities. Valuation allowances are established to reduce deferred tax assets where, based upon the available evidence, the Company concludes that it is more-likely-than-not that the deferred tax assets will not be realized. In evaluating its ability to recover deferred tax assets, the Company considers all available positive and negative evidence, including its operating results, ongoing tax planning and forecasts of future taxable income.

Reserves are provided for tax benefits for which realization is uncertain. Such benefits are only recognized when the underlying tax position is considered more-likely-than-not to be sustained on examination by a taxing authority. Interest and penalties related to uncertain tax positions are recognized in the provision of income taxes.

Comprehensive Income (Loss)

Comprehensive income (loss) includes net income (loss) as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with equity holders. For the year ended December 31, 2022, the comprehensive loss consisted of unrealized losses on available for sale investments. The Company did not have any items of comprehensive income or loss other than net income (loss) for the years ended December 31, 2021 and 2020.

Net Income (Loss) Per Share Attributable to Common Stockholders

Basic net income (loss) per share attributable to common stockholders is computed by dividing the net income (loss) attributable to common stockholders by the weighted average number of shares of common stock outstanding for the period. Diluted net income per share attributable to common stockholders is computed by dividing the diluted net income attributable to common stockholders by the weighted average number of common shares outstanding for the period, including potential dilutive common shares assuming the dilutive effect of outstanding stock options.

Prior to the Company's IPO, basic and diluted net loss per share attributable to common stockholders was determined using the two-class method, which is required for participating securities. The Company considered its convertible preferred stock to be participating securities as, in the event a dividend is paid on common stock, the holders of convertible preferred stock would be entitled to receive dividends on a basis consistent with the common stockholders. Under the two-class method, the net loss attributable to common stockholders is not allocated to the convertible preferred stock as the holders of the convertible preferred stock do not have a contractual obligation to share in losses.

Under the two-class method, basic net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock. Due to net loss for the year ended December 31, 2022 and 2020, basic and diluted net loss per share attributable to common stockholders was the same, as the effect of all potentially dilutive securities would have been anti-dilutive.

In-process Research and Development Assets

In-process research and development assets that are acquired in a transaction that does not qualify as a business combination under GAAP and that do not have an alternative future use are expensed in the period in which the assets are acquired.

Segments

Operating segments are defined as components of an entity for which separate financial information is available and that is regularly reviewed by the chief operating decision maker ("CODM"), in deciding how to allocate resources to an individual segment and in assessing performance. The Company's CODM is its chief executive officer, who manages and allocates resources to the operations on a total company basis. Accordingly, there is a single operating segment and one reportable segment.

Recently Issued Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standard Board ("FASB") or other standard setting bodies that the Company adopts as of the specified effective date. Unless otherwise disclosed below, the Company does not believe that the adoption of recently issued standards have or may have a material impact on its consolidated financial statements and disclosures.

Recently Adopted Accounting Pronouncements

The Company did not adopt any accounting pronouncements during the year ended December 31, 2022.

3. Collaboration Revenue

Background

In October 2020, the Company entered into a License Agreement ("Roche License Agreement") with F. Hoffmann-LaRoche Ltd. and Genentech, Inc. (together, "Roche") under which the Company granted an exclusive license for certain development and commercialization rights related to bemnifosbuvir outside of the United States (other than for certain HCV uses) to Roche.

In November 2021, Roche provided the Company with a notice of termination of the Roche License Agreement which became effective in February 2022. Upon termination, the rights and licenses granted by the Company to Roche under the Roche License Agreement were returned to the Company, resulting in the Company having all rights to continue the clinical development and future commercialization of bemnifosbuvir worldwide. Global development plan activities and related cost sharing between the parties continued through the effective date of the termination.

The Company concluded that the notice of termination represented a contract modification for accounting purposes. The Company further concluded that upon receipt of the notice of termination, all of the Company's performance obligations had been completely satisfied. As a result, the Company recognized all remaining deferred revenue as collaboration revenue within the consolidated statements of operations and comprehensive income (loss) for the year ended December 31, 2021.

Prior to receipt of the termination notice, the Company classified all revenues recognized under the Roche License Agreement as collaboration revenue within the accompanying consolidated statements of operations and comprehensive income (loss). The Company recorded revenue of $351,367 and $48,633 for the years ended December 31, 2021 and 2020, respectively, related to the Roche License Agreement.

The activities to complete the global development plan were accounted for under ASC 808. Expenses incurred and reimbursements made or received from Roche were accounted for pursuant to ASC 730, *Research and Development*. As such, the Company was expensing costs as incurred, including any reimbursements made to Roche, and recognizing reimbursement received from Roche as a reduction of research and development expense through the effective date of the termination.

For the years ended December 31, 2021 and 2020, costs reimbursable by Roche, which are reflected as a reduction to research and development expenses were $7,264 and $7,901, respectively. The Company recorded research and development expense of $76,567 and $2,086 during the years ended December 31, 2021 and 2020, respectively, related to its share of costs incurred by Roche. As of December 31, 2021, the Company recorded accrued expenses of $10,417 related to amounts payable to Roche.

For the year ended December 31, 2022, the Company recorded a net credit of $6,898 from Roche. The credit recorded during the year ended December 31, 2022 represents a change in estimate as a result of close out activities and related reporting of amounts incurred by Roche associated with the global development plan. Included in prepaid expenses and other current assets as of December 31, 2022 is a net balance due from Roche of $1,060.

4. Fair Value Measurements

The following tables present information about the Company's financial assets measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values:

	As of December 31, 2022			
	Level 1	Level 2	Level 3	Total
Cash equivalents				
Money market funds	$ 167,584	$ —	$ —	$ 167,584
Marketable Securities				
U.S. Treasury obligations	—	59,118	—	59,118
U.S. Government agency securities	—	14,941	—	14,941
Commercial paper	—	310,433	—	310,433
Corporate bonds	—	61,249	—	61,249
Asset-backed securities	—	12,508	—	12,508
Total	$ 167,584	$ 458,249	$ —	$ 625,833

	As of December 31, 2021			
	Level 1	Level 2	Level 3	Total
Cash equivalents				
Money market funds	$ 731,767	$ —	$ —	$ 731,767
Total cash equivalents	$ 731,767	$ —	$ —	$ 731,767

The Company's assets with fair value categorized as Level 1 within the fair value hierarchy include money market accounts which invest in money market funds that are publicly traded mutual funds and are presented as cash equivalents on the consolidated balance sheets as of December 31, 2022 and 2021.

There were no transfers among Level 1, Level 2 or Level 3 categories in the years ended December 31, 2022 and 2021.

5. Marketable Securities

	As of December 31, 2022			
	Amortized Cost	Unrealized Gain	Unrealized Losses	Fair Value
Marketable Securities				
U.S. Treasury obligations	$ 59,422	$ —	$ (304)	$ 59,118
U.S. Government agency securities	15,000	—	(59)	14,941
Commercial paper	310,433	—	—	310,433
Corporate bonds	61,504	—	(255)	61,249
Asset-backed securities	12,574	—	(66)	12,508
Total	$ 458,933	$ —	$ (684)	$ 458,249

As of December 31, 2022, the Company held 15 securities that were in an unrealized loss position of $684 with an aggregate fair value of $143,221. The Company has the intent and ability to hold such securities until recovery. As a result, the Company did not record any charges for credit-related impairments for its marketable debt securities for the year ended December 31, 2022. The Company had no marketable securities prior to July 2022.

As of December 31, 2022, none of the securities had remaining maturities longer than one year. The Company did not hold any marketable securities as of December 31, 2021.

The Company received proceeds of $91,885 from sales and maturities of marketable securities during the year ended December 31, 2022.

6. Property and Equipment, net

Property and equipment, net, consist of the following:

	December 31,	
	2022	**2021**
Laboratory equipment	$ 5	$ 5
Office furniture and fixtures	396	13
Computer hardware	102	37
Leasehold improvements	1,475	129
Total property and equipment, at cost	1,978	184
Less: accumulated depreciation and amortization	(273)	(161)
Property and equipment, net	$ 1,705	$ 23

Depreciation and amortization expense was $260, $29 and $19 for the years ended December 31, 2022, 2021 and 2020, respectively.

7. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following:

	December 31,	
	2022	**2021**
Research and development, including manufacturing and clinical expenditures	$ 7,667	$ 18,080
License fee	—	25,000
Income taxes	99	2,572
Payroll and payroll related	6,459	4,209
Professional fees and other	981	2,291
Total accrued expenses and other current liabilities	$ 15,206	$ 52,152

8. Commitments and Contingencies

Operating Lease Agreements

In July 2021, the Company entered into a non-cancelable operating lease agreement pursuant to which the Company leased office space in Boston, Massachusetts at 225 Franklin Street ("225 Lease"). The 225 Lease commencement date was January 1, 2022 and the 225 Lease runs through December 31, 2026. The 225 Lease does not contain any options for renewal or extension. The Company began to occupy the space in May 2022. Previously, the Company's principal office was located at 125 Summer Street in Boston, Massachusetts pursuant to a lease that expired in July 2022.

In connection with the 225 Lease commencement, the Company recorded a right-of-use asset and operating lease liability of $2,938 and $2,873 as of January 1, 2022. As of January 1, 2021, the date of adoption of ASC 842, the Company utilized operating classification for its former facility lease and recorded a right-of-use asset and lease liability related to its former office lease at 125 Summer Street.

The following assets and liabilities are recorded on the Company's consolidated balance sheet as of December 31, 2022 and 2021.

	As of December 31,	
	2022	2021
Right-of-use asset	$ 2,389	$ 161
Current lease liability	721	197
Non-current lease liability	2,403	—

The components of the lease allocated between the general and administrative and the research and development expenses on the consolidated statement of operations for the years ended December 31, 2022 and 2021 were as follows:

	Year Ended December 31,	
	2022	2021
Operating lease costs	$ 811	$ 281
Variable lease costs	78	37
Total lease costs	$ 889	$ 318

The variable lease costs for the years ended December 31, 2022 and 2021 include common area maintenance and other operating charges associated with the Company's lease of its principal office facilities in Boston, MA. As the Company's lease does not provide an implicit rate, the Company utilized its incremental borrowing rate to discount lease payments, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment.

	As of December 31,	
	2022	2021
Remaining lease term (in years)	4.0	0.5
Discount rate	3.1 %	7.0 %

Future minimum payments under the 225 Lease, currently the Company's only operating lease as of December 31, 2022 were as follows:

2023	$ 805
2024	821
2025	838
2026	855
Total lease payments	3,319
Less amount representing implied interest	(195)
Total lease liability	$ 3,124
Current portion of operating lease liabilities	721
Noncurrent portion of operating lease liabilities	$ 2,403

Rent expense recognized under all operating leases was $811, $318 and $303 for the years ended December 31, 2022, 2021 and 2020, respectively.

The Company is required to maintain a letter of credit for the duration of the 225 Lease. The Company maintains a bank deposit of $198, to collateralize the letter of credit which is classified as restricted cash and a long-term asset in the consolidated balance sheet as of December 31, 2022.

License Agreement

Background

In December 2021, the Company entered into a license agreement with MSD International GmbH, an affiliate of Merck & Co, Inc. (“Merck”) (“Merck License Agreement”) for the development, manufacture and commercialization of ruzasvir (“Compound”). Ruzasvir is the NS5A inhibitor the Company is developing in combination with bemnifosbuvir for the treatment of HCV.

Pursuant to the terms of the Merck License Agreement, the Company obtained from Merck an exclusive (subject to certain reserved rights to conduct internal research), sublicensable, and worldwide license under certain Merck patents and know-how to research, develop, manufacture, have manufactured, use, import, export, sell, offer for sale, and otherwise commercialize the Compound, or products containing the Compound (each a “Product”) for all therapeutic or prophylactic uses in humans (“Field”).

In consideration for the rights the Company acquired under the Merck License Agreement, the Company paid Merck a non-refundable upfront payment in the amount of $25,000 in February 2022 and will be required to pay Merck milestone payments up to $135,000 in the aggregate upon its achievement of certain development and regulatory milestones and up to $300,000 in the aggregate upon its achievement of certain sales-based milestones. Additionally, the Company will pay Merck tiered royalties based on annual net sales of Products ranging from high single digits to mid-teens percentages. The Company’s royalty payment obligations will continue until the later of (i) the expiration of the last to expire valid claim of a licensed Merck patent claiming such Product (or a Compound contained in such Product) and (ii) a period of years after the first commercial sale of such Product in such country. The Company may terminate the Merck License Agreement for convenience upon prior written notice. The first potential milestone would be payable upon the commencement of a Phase 3 clinical trial.

The Company recognized, as research and development expense, the $25,000 non-refundable upfront payment amount as a cost of the asset acquired in the year ended December 31, 2021 because the in-process research and development asset does not have an alternative future use. The upfront payment, paid in February 2022, was included in accrued expenses as of December 31, 2021.

Contingent Consulting Fee

The Company has an agreement with a consultant that requires payment of a success fee calculated as a percentage of certain product sales, subject to a cumulative maximum payout of $5.0 million. This success payment is contingent upon the occurrence of future events and the timing and likelihood of such payment is neither probable nor estimable.

Indemnification

The Company enters into certain types of contracts that contingently requires the Company to indemnify various parties against claims from third parties. These contracts primarily relate to (i) the Company’s bylaws, under which the Company must indemnify directors and executive officers, and may indemnify other officers and employees, for liabilities arising out of their relationship, (ii) contracts under which the Company must indemnify directors and certain officers and consultants for liabilities arising out of their relationship, and (iii) procurement, service or license agreements under which the Company may be required to indemnify vendors, service providers or licensees for certain claims, including claims that may be brought against them arising from the Company’s acts or omissions with respect to the Company’s products, technology, intellectual property or services.

From time to time, the Company may receive indemnification claims under these contracts in the normal course of business. In the event that one or more of these matters were to result in a claim against the Company, an adverse outcome, including a judgment or settlement, may cause a material adverse effect on the Company’s future business, operating results or financial condition. It is not possible to determine the maximum potential amount payable under these contracts since the Company has no history of prior indemnification claims and the unique facts and circumstances involved in each particular claim will be determinative.

9. Preferred Stock

As of December 31, 2022 the Company has 10,000,000 shares of preferred stock authorized. None of these shares of preferred stock have been issued.

In May 2020, the Company authorized 15,313,382 shares of Series D convertible preferred stock ("Series D Preferred") and 8,973,261 shares of Series D-1 convertible preferred stock ("Series D-1 Preferred"). In May 2020 the Company entered into a stock purchase agreement with certain investors and issued 15,313,382 shares of Series D Preferred for net proceeds of $106,631. In October 2020, the Company issued 8,973,261 shares of Series D-1 Preferred at a purchase price of $11.98 per share for aggregate net proceeds of $107,485.

In connection with the Company's IPO, all shares of its convertible preferred stock converted into 57,932,090 shares of common stock.

10. Common Stock

As of December 31, 2022, the authorized capital of the Company included 300,000,000 shares of common stock, of which 83,287,639 shares of common stock were issued and outstanding.

On all matters to be voted upon by the holders of common stock, holders of common stock are entitled to one vote per share. The holders of common stock are entitled to receive dividends, when declared by the board, and to share ratably in the Company's assets legally available for distribution to the holders of the Company's stock in the event of liquidation. The holders of common stock have no preemptive, redemption or conversion rights.

As of December 31, 2022, the Company had the following reserved shares of common stock:

Outstanding options	13,632,278
Outstanding restricted stock units	161,750
Outstanding performance-based restricted stock units	724,970
Shares reserved for future grant under 2020 Incentive Award Plan	7,961,066
Shares reserved under ESPP	1,157,964
	23,638,028

11. Stock-based Compensation

In October 2020, the Company's shareholders approved the Company's 2020 Incentive Award Plan ("2020 Plan"). The 2020 Plan initially provided for the issuance of up to 7,924,000 shares of common stock and for the grant of incentive stock options or other incentive awards to employees, officers, directors and consultants of the Company. The number of shares of common stock that may be issued under the 2020 Plan is also subject to increase on the first day of each calendar year equal to the lesser of i) 5% of the aggregate number of shares of common stock outstanding on the final day of the immediately preceding calendar year or ii) such smaller number of shares as is determined by the board of directors. Through December 31, 2022, the shares available under the plan were increased by 8,285,983 shares. As of December 31, 2022 there were 7,961,066 shares of common stock remaining available for future issuance under the 2020 Plan. In January 2023, the shares of the Company's common stock available under the 2020 Plan were increased by 4,164,381 shares.

The 2020 Plan replaced and is the successor of the Company's 2013 Equity Incentive Plan, as amended ("2013 Plan"). Upon any cancellation of outstanding option awards to purchase up to 5,982,266 shares of common stock under the 2013 Plan, such shares will be made available for grant under the 2020 Plan.

Restricted Stock Units

During the year ended December 31, 2022, the Company granted 182,350 restricted stock units to employees with an aggregate grant date fair market value of $1,302. The restricted stock unit awards vest in three annual installments, the first of which occurred on January 31, 2023. No restricted stock units were granted during the years ended December 31, 2021 and 2020. During the year ended December 31, 2022, 20,600 restricted stock units were cancelled due to terminations.

	Number of Shares		Weighted Average Grant Date Fair Value
Outstanding at January 1, 2022	—	$	—
Granted	182,350	$	7.14
Release	—	$	—
Cancelled	(20,600)	$	7.14
Unvested shares at December 31, 2022	161,750	$	7.14

Performance-based Restricted Stock Units

During the year ended December 31, 2022, the Company granted 742,070 performance-based restricted stock units to employees with an aggregate grant date fair value of $5,298. No performance-based restricted stock units were granted during the years ended December 31, 2021 and 2020. The performance stock unit awards provide for a performance period from February 1, 2022 through January 31, 2025 to achieve up to six defined performance metrics. The percentage of each award eligible to vest will be determined based on the number of metrics achieved during the performance period and may range from 0% to 200%. The Company has not recognized any compensation expense through December 31, 2022, as the minimum performance criteria had not been deemed probable. The vesting of any eligible awards will occur in equal installments on January 31, 2025 and January 31, 2026.

During the year ended December 31, 2022, 17,100 performance-based restricted stock units were cancelled due to terminations.

	Number of Shares		Weighted Average Grant Date Fair Value
Outstanding at January 1, 2022	—	$	—
Granted	742,070	$	7.14
Release	—	$	—
Cancelled	(17,100)	$	7.14
Unvested shares at December 31, 2022	724,970	$	7.14

Employee Stock Purchase Plan

In October 2020, the Company's shareholders approved the ESPP, which became effective upon the closing of the Company's IPO in November 2020. The Company initially reserved a total of 1,187,000 shares of its common stock for issuance under the ESPP. The ESPP provides that the number of shares reserved and available for issuance under the ESPP will be increased on January 1 of each calendar year by 1% of the number of shares of the Company's common stock issued and outstanding on the immediately preceding December 31 or such lesser amount as specified by the board of directors. Through December 31, 2022, there was no increase in the number of shares reserved for issuance under the ESPP. In January 2023, the number of shares of the Company's common stock available for issuance under the ESPP was increased by 832,876 shares.

In April 2022, the Company initiated its first offering period under the ESPP. Each offering period is six months in duration with the purchase date being the last trading day of the offering period. On September 30, 2022, the first offering period concluded and the Company issued 29,036 shares of its common stock for proceeds of $140.

Stock Options

The following summarizes stock option activity:

	Number of Shares	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value ($000s)
Outstanding at January 1, 2022	10,516,972	$ 22.87	8.1	$ 31,239
Granted	3,884,917	$ 7.08		
Exercised	(155,873)	$ 1.48		
Cancelled	(613,738)	$ 25.87		
Outstanding at December 31, 2022	13,632,278	$ 18.48	7.7	$ 10,937
Vested and expected to vest at December 31, 2022	13,632,278	$ 18.48	7.7	$ 10,937
Vested and exercisable at December 31, 2022	7,459,247	$ 16.11	7.0	$ 10,348

The aggregate intrinsic value of options granted is calculated as the difference between the exercise price of the options and the estimated fair value of the Company's common stock for those options that had exercise prices lower than the fair value of the Company's common stock.

Option grants generally vest over a service period of three or four years and have a contractual term of ten years. As of December 31, 2022, total unrecognized compensation expense related to stock option awards was $92,798, which amount is being recognized over a remaining weighted average period of 2.3 years.

The weighted average grant date fair value per option granted during the years ended December 31, 2022, 2021 and 2020 was $5.09, $39.10 and $14.93, respectively. The fair value of each award was estimated using Black-Scholes based on the following assumptions:

	For the Year Ended December 31,		
	2022	2021	2020
Risk-free interest rate	2.10%	0.80%	0.31 - 0.56%
Expected term	5.96 years	5.99 years	6.25 years
Expected volatility	85.0%	85.0%	80.0% - 91.7%
Expected dividend yield	0%	0%	0%

Stock-based Compensation Expense

Stock-based compensation expense is classified as follows:

	For the Year Ended December 31,		
	2022	2021	2020
Research and development expense	$ 21,870	$ 18,127	$ 3,565
General and administrative	24,848	21,494	3,892
Total stock-based compensation expense	$ 46,718	$ 39,621	$ 7,457

The components of stock-based compensation expense were:

	For the Year Ended December 31,		
	2022	2021	2020
Restricted common stock	$ —	$ —	$ 657
Restricted stock units	352	—	—
Performance-based restricted stock units	—	—	—
Stock options	46,220	39,621	6,800
ESPP	145	—	—
Total stock-based compensation expense	$ 46,718	$ 39,621	$ 7,457

12. Income Taxes

For the year ended December 31, 2022, the Company recorded a benefit for income taxes of $3,590. The benefit for income taxes was primarily the result of changes in estimates between the Company's initial provision for 2021 income taxes and the actual amounts reflected in the income tax returns as filed. For the year ended December 31, 2021, the Company recorded a provision for income taxes of $17,400.

The reconciliation of federal statutory income tax rate to the Company's effective income tax rate is as follows:

	For the Year Ended December 31,		
	2022	2021	2020
Expected income tax benefit at the federal statutory rate	21.0 %	21.0 %	21.0 %
State and local taxes	5.6	3.2	(2.6)
Return to provision adjustments	3.4	—	—
Research and development credits	2.1	(4.1)	12.5
Stock-based compensation	(3.8)	—	(13.6)
Foreign derived intangible income	-	(6.1)	—
Uncertain tax positions	(0.2)	4.3	—
Other	0.3	(1.4)	—
Change in valuation allowance	(25.3)	(4.4)	(17.3)
Total	3.1 %	12.5 %	0.0 %

Deferred income taxes reflect the net effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The principal components of the Company's deferred tax assets consisted of the following:

	December 31,	
	2022	2021
Deferred tax assets (liabilities)		
Capitalized research and development	$ 14,305	$ —
Net operating loss carryforwards	5,590	—
License agreement	6,043	6,261
Stock-based compensation	12,215	5,643
Research and development credits	3,826	—
Other	70	256
Prepaid expenses	(893)	(1,256)
Deferred tax assets (liabilities)	41,156	10,904
Less: valuation allowance	(41,156)	(10,904)
Net deferred tax assets (liabilities)	$ —	$ —

As required by the 2017 tax Cut and Jobs Act, effective January 1, 2022, our research and development expenditures were capitalized and amortized, which resulted in deferred tax asset.

As of December 31, 2022, the Company had federal net operating losses of $19,392 and state net operating loss carryforwards of $30,030, which may be used to offset future tax liabilities. The Company has federal and state credit carryforwards of $2,533 and $1,294, respectively. The federal net operating losses and research and development tax credits begin to expire in 2034.

Management has evaluated the positive and negative evidence bearing upon the realizability of the Company's deferred tax assets. Based on the Company's projected net operating losses for 2023 and beyond, the Company determined that it is more likely than not that it will not recognize the benefits of the deferred tax assets. As a result, the Company has recorded a full valuation allowance of approximately $41,156 at December 31, 2022.

Under the provisions of Sections 382 and 383 of the Internal Revenue Code ("IRC"), net operating loss and credit carryforwards and other tax attributes may be subject to limitation if there has been a significant change in ownership of the Company, as defined by the IRC.

The Company performed an analysis through December 31, 2021 pursuant to Section 382 of the IRC to determine whether any limitations might exist on the utilization of net operating losses and other tax attributes. Based on this analysis, the Company has determined that there was no impact on the Company's ability to utilize net operating losses or credit carryforwards in 2021. The Company is in the process of completing a Section 382 study for the fiscal year 2022. To the extent that the Company raises additional equity financing or other changes in the ownership interest of significant stockholders occurs, additional tax attributes may become subject to an annual limitation. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities.

The Company files federal and various state income tax returns. The statute of limitations for assessment by the Internal Revenue Service ("IRS"), and state tax authorities remains open for all tax years ended since the inception of the Company. 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 IRS or state tax authorities to the extent utilized in a future period. No federal or state tax audits are currently in process.

The Company evaluates tax positions for recognition using a more-likely-than-not recognition threshold, and those tax positions eligible for recognition are measured as the largest amount of tax benefit that is greater than 50% likely of being realized upon the effective settlement with a taxing authority that has full knowledge of all relevant information. During the year ended December 31, 2021, the Company recorded an unrecognized tax benefit of $5,932 related to certain tax positions. The Company did not have any unrecognized tax benefits prior to the year ended December 31, 2021.

The following table summarizes the reconciliation of the beginning and ending amount of total unrecognized tax benefits for the year ended December 31, 2022:

Balance beginning of year	$ 5,932
Decrease related to current year provision to return adjustment	(943)
Increase related to accrued interest	266
Balance at end of period	$ 5,255

13. Net Income (Loss) Per Share Attributable to Common Stockholders

Basic and diluted earnings per share are calculated as follows:

	Year Ended December 31,		
	2022	**2021**	**2020**
Net income (loss)	$ (115,909)	$ 121,190	$ (10,947)
Weighted average common shares outstanding, basic	83,245,385	82,820,037	21,592,441
Dilutive effect of outstanding stock options	—	5,429,206	—
Weighted average common shares outstanding, diluted	83,245,385	88,249,243	21,592,441
Net income (loss) per share, basic	$ (1.39)	$ 1.46	$ (0.51)
Net income (loss) per share, diluted	$ (1.39)	$ 1.37	$ (0.51)

Stock options for the purchase of 13,632,278 weighted average shares were excluded from the computation of diluted net loss per share attributable to common stockholders for the year ended December 31, 2022 as their effect is antidilutive.

Stock options for the purchase of 3,661,548 weighted average shares were excluded from the computation of diluted net income per share attributable to common stockholders for the year ended December 31, 2021 because those options had an anti-dilutive impact due to the assumed proceeds per share using the treasury stock method being greater than the average fair value of the Company's common shares for the period.

For the year ended December 31, 2020, options to purchase 7,917,783 shares of common stock have been excluded from the calculation of diluted net loss per share, as their effect is anti-dilutive.

14. Benefit Plan

During the year ended December 31, 2021, the Company implemented a defined contribution plan under Section 401(k) of the Internal Revenue Code ("401(k) Plan"). The 401(k) Plan covers substantially all employees who meet minimum age and service requirements. Under the terms of the 401(k) Plan, the Company records matching contributions up to 4% of the participant's eligible compensation. During the years ended December 31, 2022 and 2021, the Company recognized expense of $541 and $272, respectively, relating to matching contributions to the 401(k) Plan.

15. Related Party Transactions

During the year ended December 31, 2021, the Company entered into a consulting agreement with an entity controlled by one of its directors. The agreement provides for an annual retainer of $110. The Company recognized expense in the amount of $110 and $67 for the years ended December 31, 2022 and 2021.

In May 2022, the Company entered into a consulting agreement with one of its directors. The Company recognized expense of $1 in connection with this consulting agreement for the year ended December 31, 2022.