



**Enanta**  
Pharmaceuticals  
Great Chemistry Cures



**Annual Report 2022**





At Enanta, our commitment to developing groundbreaking medicines extends beyond our deep expertise in virology. Underlying our work is a responsibility and commitment

to transform the lives of patients with curative therapies. Personally, I am excited to see what we can accomplish in 2023 and beyond.

We are proud of our robust, wholly-owned, clinical-stage pipeline, where we are building an industry-leading respiratory virus treatment portfolio. 2022 brought significant advancements in our COVID-19 and respiratory syncytial virus (RSV) programs.

Our COVID-19 program is a natural extension of our core expertise in respiratory virology. As the global COVID-19 pandemic evolves and novel variants of SARS-CoV-2 continue to emerge, there is a strong need for conveniently-dosed, oral therapeutics. EDP-235, Enanta's orally-dosed inhibitor of coronavirus 3CL protease, which is effective across all SARS-CoV-2 variants tested *in vitro* to date, is in Phase 2 clinical testing for the treatment of COVID-19. It is designed to be a once-daily treatment without the requirement for ritonavir boosting.

In July 2022, we announced results from our Phase 1 study of EDP-235 which demonstrated that 200 mg or 400 mg once-daily dosing achieved favorable safety, tolerability, and pharmacokinetics. These data supported our advancement of EDP-235, and in November we initiated SPRINT (SARS-Cov-2 **PR**otasease **INH**ibitor **T**reatment), a Phase 2 study in non-hospitalized, symptomatic adults with mild or moderate COVID-19. The study is designed to evaluate the safety, tolerability, and antiviral activity of 200 mg and 400 mg once-daily doses of EDP-235 compared to placebo. We are confident in EDP-235 as a differentiated and much-needed treatment and expect to report data from SPRINT in the first half of 2023.

This month we announced a new research program focused on the discovery and development of inhibitors of the SARS-CoV-2 papain-like protease (PLpro) for the oral treatment of COVID-19. PLpro is an essential enzyme which, along with 3CL protease (3CLpro, or Mpro), plays an important role in viral replication and acts to suppress innate immune response. As this mechanism is distinct from 3CL protease, a PLpro inhibitor has the potential to be used alone or in combination with a 3CL protease inhibitor, such as EDP-235 or other compounds, to provide a range of treatment regimens for different patient populations suffering from COVID-19.

Our pipeline also includes EDP-938, the only RSV N-protein inhibitor in later stage clinical development. EDP-938 is being evaluated in a broad clinical program consisting of three Phase 2 trials in high-risk patient populations: RSVHR, a Phase 2b study in adults at high risk for complications from RSV; RSVPEDs, a Phase 2 study in pediatric RSV patients; and RSVTx, a Phase 2b study in adult hematopoietic cell transplant recipients with RSV.

In May, we reported top-line data from RSV-P, a Phase 2 study in community-acquired RSV infection in an otherwise healthy adult population. While the primary endpoints were not met, the study produced a key finding: the viral load and symptoms already had peaked and were declining at the time of the first dose, indicating RSV infection resolves quickly in this otherwise healthy population. This observation supports our view that EDP-938 has the most potential to benefit those who are at high-risk for complications and, along with EDP-938's favorable safety profile, gives us the confidence to pursue our broad clinical program in patient groups with high-risk of complications from RSV.

In the last half of 2022, an early season of RSV emerged in the Northern Hemisphere as immunities had apparently waned due to social distancing with the global COVID-19 pandemic. We will continue to monitor

the increase in cases in the Northern Hemisphere to see how the season will influence our ongoing trials worldwide, as well as how this will impact the timing of future data.

In the past year, we also expanded our clinical RSV portfolio through the initiation of a first-in-human study of EDP-323, a novel RSV L-protein inhibitor. EDP-323 has the potential to be used as a monotherapy or in combination with other agents, such as EDP-938, to broaden the treatment window or the addressable patient populations. Developing both EDP-323 and EDP-938 will give Enanta a clear leadership position to treat this endemic virus that can be deadly for too many. The Phase 1 study is designed to test the safety, tolerability, and pharmacokinetics of orally-administered EDP-323. We expect to report data from this study in the first half of 2023.

Also in respiratory virology, we announced a new research program targeting human metapneumovirus (hMPV) and RSV with a single agent, which we refer to as a dual-inhibitor. In preclinical studies, these dual-inhibitors have maintained activity against multiple genotypes and strains of hMPV and RSV in a range of cell types. Our goal is to select a dual hMPV/RSV clinical candidate in the fourth quarter of 2023.

In hepatitis B virus (HBV), our vision is to develop a combination regimen to deliver a functional cure for chronic HBV patients. HBV is a global public health threat and the world's most common serious liver infection. As the high unmet need for this disease persists, we remain committed to finding a cure to help those affected by HBV. We believe a combination therapy will be the ultimate cure for chronic HBV and are pursuing internal and external opportunities for candidates to develop in combination with EDP-514, our novel HBV core inhibitor.

Enanta had \$249 million in cash and marketable securities as of September 30, 2022, our fiscal year-end. In our 2022 fiscal year, we earned approximately \$86 million in royalty revenue from AbbVie's sales of MAVYRET®/MAVIRET® (glecaprevir/pibrentasvir), which remains a leading treatment for hepatitis C virus (HCV). While sales have been somewhat flat due to the COVID-19 interruption in the care cascade for HCV patients, MAVYRET/MAVIRET has been remarkably impactful for many, curing over a million people with HCV. We expect this important drug will continue to play a critical role in treating millions still infected with HCV.

As we look ahead to 2023, we are thrilled to have a robust pipeline and multiple milestones expected over the next year. None of this would be possible without our employees. Their many achievements toward developing cures are a testament to their collaboration and continued dedication to science. And importantly, we want to thank you, our shareholders, for your ongoing support, as we continue to execute against our goal of developing impactful medicines.

Sincerely,



Jay R. Luly, Ph.D.  
*President and Chief Executive Officer*



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

**Form 10-K**

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

**For the fiscal year ended September 30, 2022**

**OR**

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

**Commission File Number 001-35839**

**ENANTA PHARMACEUTICALS, INC.**

(Exact name of registrant as specified in its charter)

**DELAWARE**  
(State or other jurisdiction of  
incorporation or organization)

**2834**  
(Primary Standard Industrial  
Classification Code Number)

**04-3205099**  
(I.R.S. Employer  
Identification Number)

**500 Arsenal Street  
Watertown, Massachusetts 02472  
(617) 607-0800**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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, par value \$0.01 per share	ENTA	NASDAQ

**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, 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. ☒

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

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant as of the last business day of the registrant's most recently completed second fiscal quarter, March 31, 2022, based on the last reported sale price of the registrant's common stock of \$71.18 per share was \$1,262,330,179. The number of shares of the registrant's Common Stock, \$0.01 par value, outstanding as of November 1, 2022 was 20,797,491 shares.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the registrant's Definitive Proxy Statement for its 2023 Annual Meeting of Stockholders scheduled to be held on March 2, 2023, which Definitive Proxy will be filed with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year end of September 30, 2022 are incorporated by reference into Part III of this Form 10-K.

As used in this Form 10-K, “Enanta,” “the Company,” “we,” “our,” and “us” refer to Enanta Pharmaceuticals, Inc., and “MAVYRET/MAVIRET” refers to AbbVie’s HCV regimen consisting of tablets of glecaprevir/pibrentasvir, except where the context otherwise requires or as otherwise indicated. MAVYRET®, MAVIRET®, VIEKIRA PAK™, VIEKIRAX™, and EXVIERA™ are trademarks of AbbVie, Inc.

#### **NOTE REGARDING FORWARD LOOKING STATEMENTS**

This Annual Report on Form 10-K contains forward-looking statements concerning our business, operations and financial performance and condition, as well as our plans, objectives and expectations for our business operations and financial performance and condition. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “aim,” “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “due,” “estimate,” “expect,” “goal,” “intend,” “may,” “objective,” “plan,” “predict,” “potential,” “positioned,” “seek,” “should,” “target,” “will,” “would,” and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about overall trends, royalty revenue trends, research and clinical development plans, liquidity and capital needs and other statements of expectations, beliefs, future plans and strategies, anticipated events or trends and similar expressions. These forward-looking statements are based on our management’s current expectations, estimates, forecasts and projections about our business and the industry in which we operate and our management’s beliefs and assumptions. These forward-looking statements are not guarantees of future performance or development and involve known and unknown risks, uncertainties and other factors that are in some cases beyond our control. As a result, any or all of our forward-looking statements in this Annual Report on Form 10-K may turn out to be inaccurate. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under “Risk Factors” and discussed elsewhere in this Annual Report on Form 10-K. These forward-looking statements speak only as of the date of this Annual Report on Form 10-K. 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. You should, however, review the factors and risks we describe in the reports we will file from time to time with the SEC after the date of this Annual Report on Form 10-K.

**ENANTA PHARMACEUTICALS, INC.**  
**ANNUAL REPORT ON FORM 10-K**  
**For the year ended September 30, 2022**

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## SUMMARY OF PRINCIPAL RISK FACTORS

*This summary briefly states the principal risks and uncertainties facing our business that could affect our common stock, which are only a select portion of those risks. A more complete statement of those risks and uncertainties is set forth in the Section 1A “Risk Factors” of this report. This summary is qualified in its entirety by that more complete statement. You should carefully read the entire statement and “Risk Factors” when considering the risks and uncertainties as part of your evaluation of an investment in our common stock.*

- **Our financial prospects for the next several years are substantially dependent upon AbbVie’s success selling MAVYRET/MAVIRET, which includes our protease inhibitor, glecaprevir, for the treatment of HCV.**
  - AbbVie may continue to experience lower sales volume in future quarters due to a reduction in diagnoses and treatment rates of HCV if doctor visits and other routine healthcare activities remain at below normal levels as a result of the COVID-19 pandemic.
  - AbbVie’s MAVYRET/MAVIRET regimen will have to continue to compete successfully against other products and therapies for HCV, including competition for exclusive arrangements with third-party payors and governmental entities as well as price competition, both in the U.S. and in other markets worldwide.
- **There are many companies developing potential therapies for RSV, SARS-CoV-2, HBV and hMPV, which may result in others discovering, developing or commercializing products before we do or doing so more successfully than we do.**
  - In most of the disease areas currently the subject of our research and development efforts, there are other companies with product candidates that are more advanced than ours.
  - If we are not “first to market” with one of our product candidates in one or more of our targeted disease indications, our competitive position could be compromised because it may be more difficult for us to obtain marketing approval for that product candidate and/or market acceptance of that product candidate as a follow-on competitor.
- **Continued changes in royalty revenue earned under our AbbVie agreement or in the level of expenses associated with our clinical development programs, or both, will cause our results of operations to fluctuate from period to period. Any continuation of the recent trend of reducing royalty revenue, combined with increasing research and development expenses in support of our advancing programs, will result in continuing operating losses in future periods unless we develop other sources of revenue.**
  - Many of the preclinical and clinical development activities required for our product candidates must be contracted out to contract research organizations, or CROs, at significant expense. We expect these expenses to increase substantially in the coming years due to our advancement of compounds into more clinical studies and any impact of inflation, which will likely result in continuing operating losses.
- **We will require substantial additional funding to achieve our goals. If we do not generate sufficient funding from our existing collaboration and any future collaborations, we will need to obtain additional funding to support our operations. A failure to obtain funding when needed could force us to delay, limit, reduce or terminate some or all of our product development efforts.**
- **Clinical drug development for viral infections and liver diseases involves a lengthy and expensive process with uncertain timelines, uncertain outcomes and evolving clinical endpoints for regulatory approvals. If clinical trials of any of our proprietary product candidates are prolonged or delayed, we may be unable to commercialize our product candidates on a timely basis.**
  - None of our product candidates in our clinical development pipeline has yet to advance beyond Phase 2 clinical trials.
  - Some of our clinical trials may be delayed due to the continuing impact of COVID-19 on the ability of trial sites to conduct their operations and recruit trial subjects, as well as its potential impact on the future incidence of RSV.
  - Changes in regulatory requirements, policies and guidelines, including guidelines specifically addressing requirements for the development of treatments for RSV, SARS-CoV-2, HBV or hMPV could also delay the time required to reach approval of one or more of our product candidates.
- **The results of clinical trials are inherently uncertain. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials, if any, including sufficient efficacy and an acceptable safety and tolerability profile.**

- Several companies in the disease areas we are seeking to address have suffered significant setbacks in advanced clinical trials due to adverse safety profiles or lack of efficacy, notwithstanding promising results in earlier studies.
- Clinical trials involving our product candidates may be suspended or terminated at any time for a number of safety-related reasons. For example, administering any product candidate to humans may produce undesirable side effects not identified in preclinical studies.
- We may choose to test any of our clinical candidates preclinically and/or clinically in combination with other compounds with different mechanisms of action. Any adverse results from such testing may have adverse consequences for the further development potential of not only the combination but also the clinical candidate itself as a monotherapy or in combination with other mechanisms of action.
- **The COVID-19 pandemic has had an impact on our business operations and it could continue to materially affect directly or indirectly, our business.**
  - The extent and severity of the continuing impact of the pandemic on our business and clinical trials will be determined largely by the extent of delays in the conduct and recruitment of current and future clinical trials, reductions in the number of patients accessing AbbVie's MAVYRET/MAVIRET HCV regimen, and disruptions in the supply chains for our research and clinical trial materials.
- **We may delay 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.**
- **We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our product candidates.**
  - We are competing to develop intellectual property in areas of small-molecule drug development that are highly competitive.
  - We cannot be certain that patents will be issued or granted with respect to our patent applications that are currently pending, or that issued or granted patents will not later be found to be invalid and/or unenforceable, be interpreted in a manner that does not adequately protect our products, or otherwise fail to provide us with any competitive advantage.
- **We rely on third parties to manufacture our clinical drug supplies, monitor, support, conduct and/or oversee clinical trials of our product candidates that we develop independently.**

## PART I

### ITEM 1. BUSINESS

#### BUSINESS

##### Overview

We are a biotechnology company that uses our robust, chemistry-driven approach and drug discovery capabilities to become a leader in the discovery and development of small molecule drugs, with an emphasis on treatments for viral infections. We discovered glecaprevir, the second of two protease inhibitors discovered and developed through our collaboration with AbbVie for the treatment of chronic infection with hepatitis C virus, or HCV. Glecaprevir is co-formulated as part of AbbVie's leading brand of direct-acting antiviral, or DAA, combination treatment for HCV, which is marketed under the tradenames MAVYRET® (U.S.) and MAVIRET® (ex-U.S.) (glecaprevir/pibrentasvir). Our royalties from our AbbVie collaboration provide us funding to support our wholly-owned research and development programs, which are primarily focused on the following disease targets:

- Respiratory syncytial virus, or RSV, the most common cause of bronchiolitis and pneumonia in young children and a significant cause of respiratory illness in older adults, with estimates suggesting that on average each year RSV leads to 3 million hospitalizations globally in children under 5 years old and 177,000 hospitalizations in the U.S. in adults over the age of 65;
- SARS-CoV-2, the virus that causes COVID-19, as well as other coronaviruses, with estimates suggesting that COVID-19 has caused over 240,000 deaths and over 1.7 million hospitalizations in the U.S. in 2022 through October 29, with comparable, or at least significant, impact in other major populations of the world and with new variants still emerging;
- Hepatitis B virus, or HBV, the most prevalent chronic hepatitis, which is estimated by the World Health Organization to affect close to 300 million individuals worldwide; and
- Human metapneumovirus, or hMPV, an important, relatively recently identified cause of respiratory tract infections, particularly in children, the elderly and immunocompromised individuals, with symptoms similar to RSV.

We had \$278.5 million in cash, cash equivalents and short-term and long-term marketable securities at September 30, 2022. In fiscal 2022, we earned \$86.2 million in product royalties on AbbVie's net sales of its HCV regimens. We expect cash flows from our continuing HCV royalties and our existing financial resources will allow us to continue to fund our wholly-owned research and development programs into approximately the fourth quarter of fiscal 2024.

##### *Our Wholly-Owned Programs*

Our primary wholly-owned research and development programs are in virology, namely RSV, SARS-CoV-2, HBV and hMPV:

- RSV: We have a clinical stage program for RSV, with two compounds in clinical trials – EDP-938 and EDP-323. EDP-938, which has Fast Track designation from the U.S. Food and Drug Administration, or FDA, is a potent N-protein inhibitor of activity of both major subgroups of RSV, referred to as RSV-A and RSV-B. It has been investigated in a Phase 2a challenge study and is currently in three ongoing Phase 2 studies, each in a different patient population. In addition, we recently announced the initiation of a Phase 1 clinical study of EDP-323, an inhibitor of the RSV L-protein.
- o EDP-938 - N-protein Inhibitor Candidate: We have studied EDP-938 in two Phase 2 studies that were designed to be proof-of-concept and exploratory to understand better viral response in the context of RSV infection. These studies were conducted in otherwise healthy adults. The first study was the challenge study, which was reported out in mid-2019. The second study, known as RSVP, was designed to confirm the challenge study findings in an adult outpatient population with community-acquired RSV infection to provide additional information on symptom alleviation and viral load decline. In May 2022, we announced topline results for RSVP, noting that EDP-938 did not meet the primary endpoint of reduction in total symptom score compared to placebo, or the secondary antiviral endpoints. However, a statistically significant difference in the number of subjects achieving undetectable RSV RNA at the end of treatment at Day 5 was observed with EDP-938 compared to placebo (p=0.033). Further, EDP-938 demonstrated a favorable safety profile, consistent with that observed in approximately 500 subjects exposed to EDP-938 to date. Based on the growing safety profile of EDP-938 and differences in the range of the course of RSV infection in higher risk populations, which have always been our target populations, EDP-938 merits continued study. We believe that EDP-938 continues to have the greatest potential to show optimal efficacy in high-risk populations, as these patients have reduced RSV immunity, which manifests in a higher and longer duration of viral load and greater disease severity, allowing a bigger window to realize the full potential of EDP-938. We are continuing to evaluate EDP-938 in high-risk populations in the following ongoing and planned clinical studies,

including pediatric patients, adult hematopoietic stem cell recipients and high-risk adults, all of which have significant unmet need:

- RSVPEDs: RSVPEDs is a Phase 2 study in pediatric patients. This dose-ranging, randomized, double-blind, placebo-controlled study, will evaluate multiple ascending doses in up to four age cohorts to determine safety, tolerability, and pharmacokinetics, as well as a second part evaluating the selected dose for antiviral activity.
- RSVTx: RSVTx is a Phase 2b study in adult hematopoietic cell transplant recipients with acute RSV infection and symptoms of upper respiratory tract infection. We plan to enroll approximately 200 adult subjects 18 to 75 years of age, within 72 hours of symptom onset, who will receive EDP-938 or placebo for 21 days and will be monitored for the incidence of lower respiratory tract complications within 28 days of enrollment.
- RSVHR: On October 3, 2022, we announced the initiation of a Phase 2b study called RSVHR in high-risk adults, including those who are older than 65 years of age and those who have asthma, chronic obstructive pulmonary disease, or COPD, or congestive heart failure. Approximately 180 patients will be treated with 800 mg of EDP-938 or placebo for five days and evaluated for 28 days thereafter. The primary endpoint of the study is time to resolution of RSV lower respiratory tract disease symptoms.
- o The prevalence of RSV has not been following any normal seasonal pattern since the COVID-19 pandemic began. The future incidence and timing of RSV infections remain highly unpredictable and thus may continue to impact enrollment in our ongoing Phase 2 RSV trials.
- o EDP-323 - L-protein Inhibitor Candidate: Our newest clinical candidate for RSV is a novel oral, direct-acting antiviral selectively targeting the RSV L-protein, a viral RNA-dependent RNA polymerase enzyme that contains multiple enzymatic activities required for RSV replication. EDP-323 has shown nanomolar potency against RSV-A and RSV-B in vitro and is not expected to have cross-resistance to other classes of inhibitors. EDP-323 has the potential to be used alone or in combination with other RSV mechanisms, such as EDP-938, to broaden the treatment window or addressable patient populations. We initiated a Phase 1 clinical study of EDP-323 in October 2022.
- COVID-19: We have been leveraging our expertise in developing protease inhibitors to discover new compounds specifically designed to target the SARS-CoV-2 virus and potentially other coronaviruses.
  - o EDP-235 – Protease Inhibitor Candidate – Our lead clinical candidate for COVID-19, EDP-235, is an oral inhibitor of coronavirus 3CL protease, also referred to as 3CLpro or the main coronavirus protease, or Mpro, which has been granted Fast Track designation by the FDA. In addition to SARS-CoV-2, EDP-235 has potent antiviral activity against other human coronaviruses, enabling the potential for a pan-coronavirus treatment, including possibly coronaviruses that may infect human populations in the future.
    - Phase 1 Study – In July 2022, we completed a Phase 1 study and reported positive topline results. This first-in-human, randomized, double-blind, placebo-controlled study enrolled healthy volunteers to evaluate the safety, tolerability, and pharmacokinetics, or PK, of oral EDP-235 in single ascending doses and multiple ascending doses for seven days, and the effect of food. Data from the Phase 1 study demonstrated EDP-235 was generally safe and well-tolerated up to 400 mg for seven days with strong exposure multiples over the EC<sub>90</sub>, which is a measure of potency, specifically the concentration of drug that results in 90% inhibition of viral replication *in vitro*. EDP-235 200 mg taken once daily with food resulted in mean trough plasma levels at steady state that were 3-fold and 7-fold over the plasma-protein-adjusted EC<sub>90</sub> for the tested Alpha variant and Omicron variant, respectively, while 400 mg resulted in levels that were 6-fold and 13-fold over the plasma-protein-adjusted EC<sub>90</sub> for the respective variants. These target exposure multiples were achieved without the need for ritonavir boosting and its associated drug-drug interactions. EDP-235 is projected to have four times higher drug levels in lung tissue compared to plasma, which would be expected to drive the 400 mg multiples to 28-fold and 52-fold for the respective variants. Adverse events were infrequent and mild.
    - Phase 2 Study – In November 2022, we initiated SPRINT (SARS-Cov-2 **P**rotease **I**nhibitor **T**reatment), a Phase 2 clinical trial of EDP-235 in non-hospitalized, symptomatic adults with mild or moderate COVID-19. This randomized, double-blind, placebo-controlled study is designed to evaluate the safety, tolerability and antiviral activity of 200 mg and 400 mg once-daily doses of EDP-235 compared to placebo. The study will enroll approximately 200 non-hospitalized, symptomatic patients with mild to moderate COVID-19 who are not at increased risk for developing severe disease. Patients will be eligible to participate if they have had symptoms for five days or less and have not received a SARS-CoV-2 vaccine or been infected with SARS-CoV-2 within 90 days of enrollment. Patients will receive EDP-235 orally with food at a dose of 200 mg or 400 mg or placebo once daily for five days. The primary objective of the study includes evaluation of safety



and tolerability, and secondary objectives include pharmacokinetics and multiple virology measures to guide dose selection for other trials.

- o We are also researching additional compounds that might be eligible to be designated for clinical development for SARS-CoV-2.
- **HBV:** Our lead clinical candidate for the treatment of chronic infection with hepatitis B virus, or HBV, is EDP-514, a core inhibitor that displays potent anti-HBV activity *in vitro* at multiple points in the HBV lifecycle. Our goal is to develop a combination therapy approach, including existing approved treatments such as a nucleoside reverse transcriptase inhibitor, or NUC, with EDP-514 and one or more other mechanisms, which could lead to a functional cure for patients with chronic HBV infection. We are in the process of seeking other compounds that could be developed with EDP-514 for such a treatment regimen.
- o **EDP-514 - Core Inhibitor Candidate** - In June 2022, final data from two of our Phase 1b studies of EDP-514 were presented at The International Liver Congress™ 2022. EDP-514, which has Fast Track designation from the FDA, has been shown to be safe and potent in two different chronic HBV patient populations – those who have a high viral load, whom we refer to as viremic patients, and those who are on a treatment with a nucleoside reverse transcriptase inhibitor, whom we refer to as NUC-suppressed patients. Based on these data, we remain convinced that EDP-514 has the potential to be a best-in-class core inhibitor for HBV.
- **hMPV:** Human metapneumovirus, or hMPV, a virus that is a significant cause of respiratory tract infections, or RTIs, particularly in children, the elderly and immunocompromised individuals. It is the second most common cause of lower respiratory tract infections in children, with symptoms similar to RSV. The viral structure and lifecycle of hMPV are also similar to RSV. We have been optimizing nanomolar inhibitor leads against hMPV and are working toward selecting our first development candidate for this indication in 2023.

We have utilized our internal chemistry and drug discovery capabilities to generate all of our development-stage programs. We continue to invest substantial resources in research programs to discover back-up compounds as well as new compounds targeting different mechanisms of action, both in our disease areas of focus as well as potentially in other disease areas.

### ***Our Out-Licensed Products***

**HCV:** Two protease inhibitors developed through our Collaborative Development and License Agreement with AbbVie have been clinically tested, manufactured, and commercialized by AbbVie as part of its combination regimens for HCV. We have received the full \$330.0 million of contractual milestone payments under the agreement related to clinical development and commercialization regulatory approvals of these regimens in major markets, and we continue to earn royalties on sales of those regimens.

Glecaprevir is the HCV protease inhibitor we discovered that was developed by AbbVie in a fixed-dose combination with its NS5A inhibitor, pibrentasvir, for the treatment of chronic HCV. This patented combination, currently marketed under the brand names MAVYRET® (U.S.) and MAVIRET® (ex-U.S.), is referred to in this report as MAVYRET/MAVIRET. This regimen is a once-daily, all-oral, fixed-dose, ribavirin-free treatment for HCV genotypes 1-6, or GT1-6, which is referred to as being pan-genotypic. In the U.S., EU and Japan it is approved as an 8-week treatment for patients with and without compensated cirrhosis and new to treatment. Today, these patients are estimated to represent the majority of HCV patients in over 50 countries where MAVYRET/MAVIRET is sold by AbbVie and where MAVYRET/MAVIRET remains the only 8-week pan-genotypic HCV treatment. The first protease inhibitor developed through this collaboration, paritaprevir, is part of Abbvie's initial HCV regimens, which have been almost entirely replaced by MAVYRET/MAVIRET. Since August 2017, substantially all of our royalty revenue has been derived from AbbVie's net sales of MAVYRET/MAVIRET. Our ongoing royalty revenues from this regimen consist of annually tiered, double-digit, per-product royalties on 50% of the calendar year net sales of the 2-DAA glecaprevir/pibrentasvir combination in MAVYRET/MAVIRET. The annual royalty tiers return to the lowest tier for sales on and after each January 1.

## Our Strategy

Our primary objective is to become a leader in the discovery and development of treatments for viral infections to provide new therapies for patients with unmet medical needs. Our principal focus is on antiviral targets for viruses such as RSV, SARS-CoV-2, HBV and hMPV, which in most cases are therapeutic areas that have attracted research and development efforts of many competitors. Our strategy includes the following key elements:

- *Advance clinical development of novel virology product candidates for RSV, SARS-CoV-2, HBV and hMPV.* We have ongoing clinical studies of three compounds discovered in our research programs in the disease areas of RSV and SARS-CoV-2. We believe each of these diseases represents a substantial medical need for an effective, or more effective, treatment.
- *Invest in research and development of compounds in new disease areas or add to our clinical candidates in RSV, SARS-CoV-2, HBV and hMPV.* We are continuing to invest significant resources in our research programs in our efforts to identify and advance additional novel compounds that have the potential to address significant unmet medical needs in our primary disease areas, as well as others. We may also explore clinically other diseases where our assets could play a role. In addition, we may seek to augment our product candidate pipeline through the acquisition or in-licensing of external assets and/or technologies in one or more of our disease areas of focus.
- *Collaborate or out-license, where and when appropriate, with pharmaceutical partners to create combination therapies and accelerate the development and commercialization of our proprietary compounds.* We are prepared to join forces, where and when appropriate, with collaborators with compounds targeting other mechanisms of action in diseases such as HBV, where there is the potential for better treatments with combination therapies. Our decisions regarding our proprietary programs will be based on the results of our early phase clinical studies and the potential for combinations with one or more drugs targeting other mechanisms of action in these diseases.
- *Continue to use our existing resources and future cash flow from our AbbVie collaboration to fund our research and development activities.* We expect our existing financial resources and future royalty payments from our AbbVie collaboration will provide us resources to fund our research and development programs into approximately the fourth quarter of fiscal 2024. These resources will allow us to continue to advance compounds in clinical development and to progress the most promising candidates at least through proof-of-concept trials. Further development of any compound as a monotherapy or in combinations with other therapeutic agents when we believe such combinations will provide the most promising opportunities will likely require additional financial resources.

## Our Research and Development Pipeline

The following table summarizes our product development pipeline in our virology and liver disease programs:

### Enanta Pipeline

	PRODUCT CANDIDATE		DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	MARKET
Virology: Liver	HCV	Protease Inhibitor	Glecaprevir-containing pangenotypic 2-DAA combo					
	HBV	Core Inhibitor	EDP-514					
Virology: Respiratory	RSV	N-Protein Inhibitor	EDP-938		RSVPEDs			
			EDP-938		RSVTx			
			EDP-938		RSVHR			
		L-Protein Inhibitor	EDP-323					
	hMPV	Non-Fusion Inhibitor						
	COVID-19	Protease Inhibitor	EDP-235		SPRINT			
Discovery or Preclinical	RSV, HBV, COVID-19, other							
For Out-license	NASH	FXR Agonists	EDP-305 (Phase 2), EDP-297 (Phase 1)					

\*Fixed-dose combination contains glecaprevir and AbbVie's NS5A inhibitor, pibrentasvir. Marketed by AbbVie as MAVYRET® (U.S.) and MAVIRET® (ex-U.S.).

## Our RSV Program

### Background and Overview of RSV

Respiratory syncytial virus, or RSV, is a virus that infects the lungs and is the most common cause of bronchiolitis and pneumonia in young children and a significant cause of respiratory illness in older adults. Almost all children are infected at least once before they are 2 years old, and about a half are infected twice, resulting in over 2 million outpatient visits in young children. Hospitalization rates due to RSV are approximately 16 times higher than for influenza among children aged less than 1 year. On average each year in the U.S., RSV leads to 58,000 hospitalizations in children under 5 years old and 177,000 in adults older than 65 years old. RSV is estimated to cause 100–500 deaths annually in children under 5 years old and 14,000 deaths in adults over 65 years old in the U.S. There are currently no safe and effective therapies for RSV infection.

### Scientific Background

RSV is a single-stranded, negative-sense RNA virus. The RSV genome consists of ten genes that encode for 11 proteins, namely NS1, NS2, N, P, M, SH, G, F, M2-1, M2-2, and L. The F and G proteins are the predominant target proteins for RSV vaccines. Similarly, small molecule therapeutics have focused primarily on the F (or fusion) protein, while some efforts have targeted the N and L proteins. There are two major subgroups of RSV, designated RSV-A and RSV-B, each of which contains numerous genotypes. Both groups are viewed as capable of causing RSV infections that can result in hospitalization.

Several companies are seeking to develop antiviral treatments for RSV infection in adult and pediatric patients. Ark Biosciences (Ziresovir – fusion inhibitor), Pfizer/ReViral (acquired in June 2022) (sinsunatovir – fusion inhibitor and RV299 – N inhibitor), and Merck (molnupiravir – polymerase inhibitor) have compounds in clinical development. Synagis, a prophylactic, monoclonal-antibody-based treatment from AstraZeneca, which is commercialized by AbbVie outside the U.S., is approved for infants considered at high risk for RSV infection; however, studies have found that most young children with RSV infection were previously healthy, and thus would not normally be prescribed prophylactic treatment. AstraZeneca/Sanofi (Beyfortus/nirsevimab – filed in U.S./EU) and Merck (clesrovimab – Phase 3) are developing long-acting versions of the monoclonal antibody for prophylaxis use in infants. In addition, a number of companies have RSV vaccines in development, primarily directed at prevention of RSV infection, and some companies are also evaluating vaccines in a therapeutic mode for treatment of established RSV infection.

## ***Our Approach to the Treatment of RSV***

While a number of companies are developing potential approaches geared toward the F protein (or fusion protein, responsible for mediating viral entry of RSV into host cells), we are focused on other mechanisms, such as the N-protein and the L-protein, that target the replication process of RSV. It is possible that N-protein and L-protein inhibitors may also be effective treatments at later stages of infection.

### ***EDP-938, Our N-Protein Inhibitor***

Through our internal chemistry efforts, we identified our lead clinical candidate, EDP-938. During preclinical studies, EDP-938 demonstrated a greater than 4-log reduction in viral load in an animal model challenged with RSV. Further, EDP-938 maintained antiviral potency across all clinical isolates tested *in vitro*, as well as virus that was resistant to fusion inhibitors. The compound inhibited RSV at a post-entry replication step and maintained its activity *in vitro* when given 24 hours post infection. In addition, combination studies of EDP-938 with other types of RSV inhibitors, such as fusion inhibitors, showed synergistic antiviral effects.

We have studied EDP-938 in two Phase 2 studies that were designed to be proof-of-concept and exploratory to better understand antiviral response in the context of RSV infection. These studies were conducted in otherwise healthy adults. The first study was a challenge study, which had a data readout in June 2019. This study was a randomized, double-blind, placebo-controlled, human challenge study of 115 healthy adult subjects. Data from this study demonstrated that EDP-938 was safe and well-tolerated and achieved highly statistically significant reductions ( $p < 0.001$ ) in RSV viral load and symptoms compared to placebo. See Ahmad et al, *N Engl J Med* 2022; 386:655-666. The second study, known as RSV-P, was designed to confirm the challenge study findings in an adult outpatient population with mild and self-resolving community-acquired, RSV infection to provide us additional information on symptom alleviation and viral load decline. In May 2022, we announced topline results for RSV-P, noting that EDP-938 did not meet the primary endpoint of reduction in total symptom score compared to placebo, or the secondary antiviral endpoints. However, a statistically significant difference in the number of subjects achieving undetectable RSV RNA at the end of treatment at Day 5 was observed with EDP-938 compared to placebo ( $p = 0.033$ ). Although patients were treated within 48 hours of symptom onset, the viral load and symptoms had already peaked and were declining, indicating RSV infection resolves quickly in this otherwise healthy population. Further, EDP-938 demonstrated a favorable safety profile, consistent with that observed in approximately 500 subjects exposed to date. Based on the growing safety profile of EDP-938 and differences in the range of the course of RSV infection in higher risk populations, which have always been our target populations, we are progressing development of EDP-938 in patients at high-risk for developing severe infection leading to hospitalization or death. EDP-938 has the greatest potential to show optimal efficacy in these high-risk populations with significant unmet need, as these patients have reduced RSV immunity, which manifests in a higher and longer duration of viral replication and greater disease severity, allowing a bigger window to realize the full potential of EDP-938.

We are now studying EDP-938 in three additional RSV studies:

- **RSVPEDs** is a Phase 2 dose-ranging, randomized, double-blind, placebo-controlled study in pediatric patients. We plan to enroll approximately 90 infants and children aged 28 days to 36 months with RSV-associated respiratory tract infection, who will be dosed in up to four age cohorts and will receive EDP-938 or a placebo for five days. The study will be conducted in two parts. Part 1 will evaluate multiple ascending doses in each age cohort, with a primary endpoint of safety, tolerability, and pharmacokinetics. Part 2 will evaluate the selected dose from Part 1 across the age cohorts, with a primary endpoint of antiviral activity.
- **RSVTx** is a Phase 2b study in adult hematopoietic cell transplant recipients with acute RSV infection and symptoms of upper respiratory tract infection. This study is designed to enroll approximately 200 adult subjects 18 to 75 years of age, within 72 hours of symptom onset, who will receive EDP-938 or placebo for 21 days. The primary endpoint is the incidence of lower respiratory tract complications within 28 days of enrollment, while secondary endpoints include change from baseline in RSV RNA viral load, safety and pharmacokinetics.
- **RSVHR** is a Phase 2b study initiated in October 2022 in high-risk adults, including those who are older than 65 years of age, have asthma, chronic obstructive pulmonary disease, or COPD, or congestive heart failure. Approximately 180 patients will be treated with 800 mg of EDP-938 or placebo for five days and evaluated for 28 days thereafter. The study will include non-hospitalized adult subjects with up to 72 hours of respiratory tract infection symptoms who test positive for RSV and negative for influenza virus and SARS-CoV-2. The primary endpoint of the study is time to resolution of RSV lower respiratory tract disease symptoms as assessed by the Respiratory Infection Intensity and Impact Questionnaire, or RiiQ™, symptom scale through Day 33. Secondary endpoints include additional clinical efficacy measures and antiviral activity compared to placebo, pharmacokinetics, and safety of EDP-938.



### ***EDP-323, Our RSV L-Protein Inhibitor:***

In addition to our N-protein inhibitor, EDP-938, our newest clinical candidate for RSV is EDP-323, a novel oral, direct-acting antiviral selectively targeting the RSV L-protein, a viral RNA-dependent RNA polymerase enzyme that contains multiple enzymatic activities required for RSV replication. EDP-323 has shown nanomolar potency against RSV-A and RSV-B in vitro and is not expected to have cross-resistance to other classes of inhibitors. EDP-323 has the potential to be used alone or in combination with other RSV mechanisms, such as EDP-938, to broaden the treatment window or addressable patient populations.

We initiated a Phase 1 clinical study of EDP-323 in October 2022. This randomized, double-blind, placebo-controlled, first-in-human Phase 1 study will enroll approximately 80 healthy subjects ranging in age from 18 to 65 years old to evaluate the safety, tolerability and pharmacokinetics, or PK, of EDP-323 with a single-ascending dose phase, including a two-part food effect, or FE, cohort, and a multiple-ascending dose phase. All single-ascending dose, or SAD, and multiple-ascending dose cohorts will enroll eight participants who will be randomized to receive EDP-323 or placebo in a 3:1 ratio. The SAD/FE cohort will enroll ten subjects randomized in a 4:1 ratio.

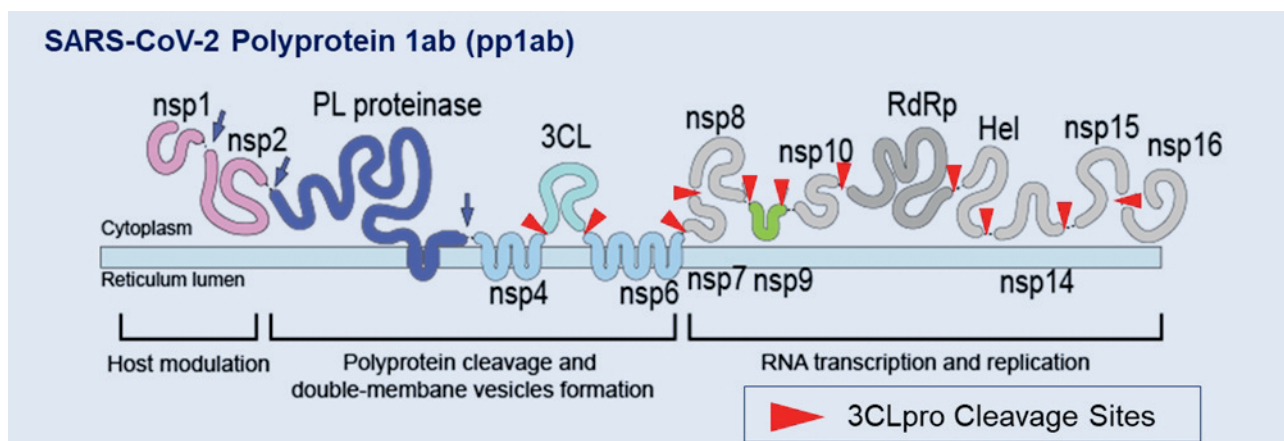
### **Our SARS-CoV-2 Program**

#### ***Background and Overview of SARS-CoV-2***

Severe acute respiratory syndrome coronavirus 2, or SARS-CoV-2, is the virus that causes COVID-19 (coronavirus disease 2019), the respiratory illness responsible for the COVID-19 pandemic. SARS-CoV-2 is the seventh known coronavirus to infect people, after 229E, NL63, OC43, HKU1, MERS-CoV, and the original SARS-CoV. Most people infected with the virus experience mild to moderate respiratory illness and recover over time. However, some patients will have more severe symptoms requiring hospitalization and may experience severe life-threatening complications, including acute respiratory distress syndrome, or ARDS, which may trigger a systemic multi-organ collapse. Older people and those with underlying medical conditions like cardiovascular disease, diabetes, chronic respiratory disease, or cancer are more likely to develop serious illness. There are also many patients who experience continuing effects of COVID-19, often referred to as “long COVID”, and there still is little known about the enduring effects of the disease. As of November 1, 2022, the World Health Organization estimated that there were approximately 620 million reported cases of people infected with SARS-CoV-2 worldwide, resulting in approximately 6.5 million deaths, while many estimates of the number of infections far exceed the reported cases. While effective vaccines are available, uptake has not been optimal. In addition, breakthrough infection can occur because the vaccines are not 100% effective, especially against emerging variants. With the continuing prevalence of COVID-19 globally, there is heightened risk of a further mutation of the virus that could evade one or more of the current vaccines. Thus, there is an urgent need for effective, safe, oral, antiviral treatments.

#### ***Scientific Background***

All coronaviruses have a single-stranded, positive-sense RNA (+ssRNA) genome, which is the largest known genome for an RNA virus. The overall structure of the SARS-CoV-2 genome is shared with other betacoronaviruses, namely MERS-CoV and SARS-CoV. These viruses encode two cysteine proteases, which are enzymes that break down, or cleave, proteins into smaller pieces and are indispensable for viral replication: 3C-like protease, or 3CLpro (also known as the main protease, or Mpro) and papain-like protease, or PLpro. 3CLpro cleaves at 11 sites in the viral polyprotein, which is required for creating 16 separate, non-structural proteins that constitute the structural complex that enables replication of the SARS-CoV-2 virus, and PLpro cleaves three other sites within the viral polyprotein as well as multiple host proteins. Due primarily to their central role in viral replication, and the previous success of strategies targeting viral proteases, 3CLpro and PLpro are highly attractive targets for the development of direct-acting antiviral agents.



Source: Derived from ViralZone 2020, SIB Swiss Institute of Bioinformatics. Retrieved from [https://viralzone.expasy.org/764?outline=all\\_by\\_species](https://viralzone.expasy.org/764?outline=all_by_species).

Early in the COVID-19 pandemic, hundreds of existing antivirals and other compounds were initially screened for activity against SARS-CoV-2 in the hopes of quickly finding an effective treatment. Some of these compounds progressed into clinical testing, including remdesivir, which is currently the only FDA-approved antiviral for COVID-19. Remdesivir was originally developed for treatment of the Ebola virus, but it showed efficacy in COVID-19. Currently, there are two Emergency Use Authorizations of oral antiviral treatments for non-hospitalized, high-risk patients with SARS-CoV-2 infection: Paxlovid, a 3CL protease inhibitor, and Molnupiravir, a polymerase inhibitor. Additionally, there are several companies developing oral direct acting antivirals for SARS-CoV-2 that are currently in Phase 2 or Phase 3 studies, including Shionogi, Gilead (an oral formulation of remdesivir), Toyama, Pardes, Atea, SyneuRx and Todos, as well as additional compounds in Phase 1 studies.

Merck reported results from a Phase 3 study of molnupiravir in high-risk outpatients infected with COVID-19, which showed a 50% reduction in hospitalization or death through one month after treatment compared to placebo. Molnupiravir is currently approved in the UK and U.S. under EUA but is limited to situations where other FDA-authorized treatments for COVID-19 are inaccessible or are not clinically appropriate. Pfizer also reported results from a Phase 3 study of Paxlovid in high-risk outpatients infected with COVID-19, which showed an 85% reduction in hospitalization or death through one month after treatment compared to placebo (89% if treated within 3 days of symptom onset). Paxlovid is dosed twice daily in combination with a low dose of ritonavir, which has significant drug interactions with numerous other medications. These data indicate the opportunity for novel SARS-CoV-2 direct-acting antivirals and highlight the need to bring forward safe, efficacious and convenient treatments. We have been leveraging our expertise in protease inhibitors to discover new compounds specifically designed to target the SARS-CoV-2 virus and potentially other coronaviruses.

**EDP-235, Our Lead, Oral, 3CL Protease Inhibitor**

Our lead clinical candidate for COVID-19 is EDP-235, an oral inhibitor of coronavirus 3CL protease, which has been granted Fast Track designation from the FDA. In addition to SARS-CoV-2, EDP-235 has potent antiviral activity against other human coronaviruses, enabling the potential for a pan-coronavirus treatment, including possibly coronaviruses that may infect human populations in the future.

In a biochemical assay, EDP-235 inhibited the SARS-CoV-2 3CL protease with an IC<sub>50</sub> of 5.8 nM. Importantly, this activity was retained against proteases from SARS-CoV-2 variants, including Omicron. EDP-235 potently blocked the replication of SARS-CoV-2 in multiple cellular models, including primary human airway epithelial cells, where an EC<sub>90</sub> of 33 nM was observed. Additionally, EDP-235 was shown to have potent antiviral activity across other human coronaviruses. In comparison to preclinical data from other direct acting antivirals in development for COVID-19 today, EDP-235 appears to be among the most potent against SARS-CoV-2 in cellular assays.

Assay		Lineage	Potency (nM)
Biochemical Activity	3CLpro FRET (IC <sub>50</sub> )	B.1.1.529, BA.2, BA.5, BA.2.75* (P132H) [Omicron]	4.1 ± 0.8
		A [Original] / B.1.617.2 [Delta]**	5.8 ± 3.7
		B.1.1.318 (T21I)	2.0 ± 0.1
		B.1.351 (K90R) [Beta]	2.8 ± 0.9
		B.1.351.2 (K90R/A193V) [Beta]	5.4 ± 1.0
		B.1.617.3 (A194S)	5.7 ± 0.5
		C.36.3 (G15S)	4.7 ± 2.5
		P.2 (L205V) [Zeta]	3.4 ± 1.0
Live Virus	Vero E6 +PGPi, CPE readout (EC <sub>90</sub> )	A [Original]	11 ± 8
		B.1.617.2 [Delta]	9.1 ± 2.9
		B.1.1.529 [Omicron]	5.1 (n=1)

FRET: fluorescence resonance energy transfer, P-gpi: P-glycoprotein inhibitor CP-100356 (2 μM), CPE: cytopathic effect

Values average of replicate experiments except where noted

\*Omicron subvariant colloquially known as ‘Centaurus’

\*\*3CLpro sequences for the ancestral A lineage and B.1.617.2 (Delta) variant are identical

EDP-235 showed good human Caco-2 cell permeability and a low plasma clearance in human liver microsomes. Consistent with this *in vitro* data, EDP-235 had robust plasma exposure with an oral bioavailability of 95% in rats. Moreover, EDP-235 had favorable *in vivo* penetration into multiple target tissues, including lung, kidney, liver, and heart. These results indicate that EDP-235 has good oral bioavailability and target tissue distribution compared to other antivirals in development for SARS-CoV-2 today. Based on allometric scaling, EDP-235 is projected to have a long half-life of 16 hours with an efficacious dose of 100 to 500 mg once-daily in humans. Taken together, these data indicate that EDP-235 has the potential for once-daily oral dosing with a low pill burden. These predictions are now supported by Phase 1 pharmacokinetic data at a 200mg and 400mg once-daily dose.

Clinical studies of EDP-235 consist of the following:

- **Phase 1 Study:** In July 2022, we completed a Phase 1 study of EDP-235 and reported positive topline results. This first-in-human, randomized, double-blind, placebo-controlled study enrolled healthy volunteers to evaluate the safety, tolerability, and pharmacokinetics, or PK, of oral EDP-235 in single ascending doses and multiple ascending doses for seven days, and the effect of food. Data from the Phase 1 study demonstrated EDP-235 was generally safe and well-tolerated up to 400 mg for seven days with infrequent adverse events, the majority of which were mild. Results demonstrated strong exposure multiples over the  $EC_{90}$ , which is a measure of potency, specifically the concentration of drug that results in 90% inhibition of viral replication *in vitro*. EDP-235 200 mg taken once daily with food resulted in mean trough plasma levels at steady state that were 3-fold and 7-fold over the plasma-protein-adjusted  $EC_{90}$  for the tested Alpha variant and Omicron variant, respectively, while 400 mg resulted in levels that were 6-fold and 13-fold over the plasma-protein-adjusted  $EC_{90}$  for the respective variants. These target exposure multiples were achieved without the need for ritonavir boosting and its associated drug-drug interactions. EDP-235 is projected to have four times higher drug levels in lung tissue compared to plasma, which would be expected to drive the 400 mg multiples to 28-fold and 52-fold for the respective variants.
- **Phase 2 SPRINT Study:** In November 2022, we initiated SPRINT (SARS-Cov-2 **Protease Inhibitor Treatment**), a Phase 2 clinical trial of EDP-235 in non-hospitalized, symptomatic adults with mild or moderate COVID-19. This randomized, double-blind, placebo-controlled study is designed to evaluate the safety, tolerability and antiviral activity of 200 mg and 400 mg once-daily doses of EDP-235 compared to placebo. The study will enroll approximately 200 non-hospitalized, symptomatic patients with mild to moderate COVID-19 who are not at increased risk for developing severe disease. Patients will be eligible to participate if they have had symptoms for five days or less and have not received a SARS-CoV-2 vaccine or been infected with SARS-CoV-2 within 90 days of enrollment. Patients will receive EDP-235 orally with food at a dose of 200 mg or 400 mg or placebo once daily for five days. The primary objective of the study includes evaluation of safety and tolerability, and secondary objectives include pharmacokinetics and multiple virology measures to guide dose selection for other trials.

## Our HBV Program

### *Background and Overview of HBV*

Hepatitis B virus, or HBV, can cause potentially life-threatening liver infection. The virus is transmitted through contact with the blood or other bodily fluids of an infected person. It is estimated that close to 300 million people worldwide are chronically infected, and 15-40% of patients with chronic HBV infection develop chronic liver disease, including cirrhosis, liver cancer, or liver decompensation. HBV is a leading cause of chronic liver disease and need for liver transplantation. It is estimated that more than 820,000 people worldwide died in 2019 due to complications of HBV.

Current approaches to treatment include interferon therapy and/or inhibitors of HBV reverse transcriptase, the enzyme responsible for viral DNA synthesis, which is necessary for HBV replication. Treatment with interferon offers modest cure rates, and is accompanied by serious side effects, including flu-like symptoms, fatigue, headache and nausea. Reverse transcriptase inhibitors can be very effective at suppressing the virus but often require lifelong therapy and rarely result in full eradication of the virus from the liver. New treatments that can provide functional cures to chronically-infected patients are urgently needed.

### *Scientific Background*

HBV is a partially double-stranded DNA virus with a complex life cycle. There are multiple mechanisms associated with HBV replication that could potentially be targeted with new drugs, and combination approaches may ultimately provide the most effective therapy for HBV. Mechanisms under study for HBV include:

- Entry inhibitors that interfere with the initial binding of HBV to hepatocytes, thus preventing new infection from occurring.
- Inhibitors of covalently closed circular DNA, or cccDNA, the template for HBV replication, most of which act in an indirect manner, such as preventing formation of cccDNA or silencing its transcription.
- RNA silencing of gene expression (siRNA's and ASO's) has the potential to significantly reduce HBV RNA, HBV DNA, and HBV protein levels.
- Inhibition of the hepatitis B core protein, which plays a critical role in viral replication, intracellular trafficking, and maintenance of chronic infections.
- The modulators of the human immune system, or immunomodulators, are another major mechanism being researched, including agonists of toll-like receptors, modulators of apoptotic signaling, and checkpoint inhibition, as well as therapeutic vaccines.

While there are antiviral medications prescribed for HBV that can suppress HBV DNA, they generally have low cure rates, resulting in the need for lifelong treatment. Many companies are seeking to develop new HBV drugs that alone or in combination with other mechanisms could lead to a functional cure for HBV. Altimmune, Arbutus, Ascleitis, Assembly, Gilead, Green Cross, GSK/Ionis, HEC Pharma, Johnson & Johnson/Janssen, Qilu, Replicor, Roche, Vaccitech, VBI Vaccines and Vir Biotechnology have Phase 2 programs in progress, with many of these companies conducting earlier stage programs as well. In addition, several companies have Phase 1 or earlier stage HBV programs.

We believe that HBV, like HIV and HCV, will be optimally treated with multiple agents that have different mechanisms, and therefore seek to develop a combination regimen. We initially focused on new core inhibitors that we expect to have an impact on capsid assembly and possibly interfere with other viral processes. Core inhibitors, also known as capsid assembly modulators or core protein allosteric modulators, are a novel class of replication inhibitors that have been shown to act at multiple steps in the HBV lifecycle. These inhibitors are expected to prevent proper uncoating, nuclear import, assembly, and recycling. This approach is supported by clinical validation, demonstrating reduction of viral RNA and DNA in chronic HBV patients in Phase 2 clinical studies.

### **EDP-514**

EDP-514, our most advanced novel core inhibitor, displays potent anti-HBV activity *in vitro* at multiple points in the HBV lifecycle and has been studied in two Phase 1b studies in patients with chronic HBV.

- In the first study, which evaluated EDP-514 in NUC-suppressed chronic HBV patients, EDP-514 led to a maximum HBV RNA reduction of 2.3 log in HBeAg-negative and 2.8 log in HBeAg-positive subjects in the EDP-514 arms compared to 1.2 log in placebo. For the EDP-514 800 mg subjects, five of six subjects had either non-detectable or very low levels of HBV RNA at baseline; consequently, the effect of EDP-514 on HBV RNA could not be assessed in these subjects. There were no instances of virologic failure. Overall, EDP-514 was generally safe and well-tolerated at 200, 400 and 800 mg doses for 28 days in NUC-suppressed chronic HBV patients. EDP-514 was rapidly absorbed and its exposure increased with increasing multiple doses. EDP-514 exhibited PK suitable for once daily oral dosing.
- A separate Phase 1b study was conducted in patients with chronic HBV infection who were not previously on HBV therapy and had high levels of virus in their blood, whom we refer to as viremic HBV patients. Results demonstrated that EDP-514 was safe and well-tolerated through 28 days of treatment, displayed pharmacokinetics supportive of once-daily dosing. Mean HBV DNA reductions of 2.9, 3.3, and 3.5 logs were observed at 28 days for the 200 mg, 400 mg, and 800 mg cohorts, respectively, compared to 0.2 log in the placebo cohort. Mean HBV RNA reductions in the three viremic treatment cohorts were at least 2 logs compared to a 0.02 log reduction in the placebo group. Our goal is to develop a combination therapy approach, including existing approved treatments such as a NUC, with EDP-514 and one or more other mechanisms, which could lead to a functional cure for patients with chronic HBV infection. We are actively pursuing opportunities for internal or external development of this combination approach.

## **Our hMPV Program**

### **Background and Overview of hMPV**

Human metapneumovirus, or hMPV, is an important cause of acute respiratory tract infections, or RTIs, and is associated with considerable morbidity, particularly in children, the elderly and immunocompromised individuals. Broader use of molecular diagnostic testing has increased identification and awareness of hMPV as an important cause of upper and lower respiratory infection. It is the second most common cause of lower RTIs in children behind RSV. Nearly every child will be infected with hMPV by the age of 5 and reinfection occurs throughout life. Rates of hospitalization in children are highest in the first year of life but occur throughout early childhood. Many studies report the peak age of hospitalization between 6 and 12 months of age, which is later than for RSV.

In otherwise healthy younger adults, hMPV infection is typically mild, however infection leads to increased disease severity and high morbidity and mortality rates in the elderly. A retrospective study in Canada showed that 46% of hMPV cases were from patients >65 years old, and 60% of these elderly patients were hospitalized. A subsequent study reported that at least 50% of elderly patients infected during an hMPV outbreak in a long-term care facility developed bronchitis or pneumonia, leading to 50% mortality. See Shafagati N, Williams J. F1000Res. 2018 Feb 1;7:135. There are no approved vaccines or therapeutics available for hMPV.

### **Scientific Background**

hMPV is a paramyxovirus that is closely related to RSV. It is a negative-sense, non-segmented, single-stranded RNA virus. The genome is about 13,000 nucleotides with 8 genes encoding for 9 proteins, including a nucleoprotein (N), phosphoprotein (P), matrix protein (M), fusion protein (F), matrix-2 proteins (M2-1 and M2-2), small hydrophobic (SH) protein, glycoprotein (G), and large (L) polymerase protein. Though similar to RSV, hMPV has a different gene order and lacks the non-structural proteins (NS1 & NS2) of



RSV. Nucleotide analysis of hMPV's fusion (F) and glycoprotein (G) genes class hMPV into four distinct groups: A1, A2, B1, and B2. Although both genotypes A and B can co-circulate in a given community, the dominant lineage tends to vary year by year.

As in other paramyxoviruses, replication is dependent on several viral proteins (N, L, and P) that form a multiprotein viral replication complex in cells, providing multiple potential targets for drug discovery of replication inhibitors.

We have been optimizing nanomolar inhibitor leads against this virus and are working toward completing toxicology testing and selecting our first development candidate for this indication in 2023.

## **Our Out-Licensed HCV Protease Inhibitor Products**

### ***Background and Overview of HCV Market***

HCV is a virus that is a common cause of viral hepatitis, an inflammation of the liver. HCV is typically contracted by contact with the blood or other body fluids of another individual infected with HCV. HCV is a leading cause of chronic liver disease, including cirrhosis, liver failure and cancer, and the leading cause of death from liver disease in the United States. HCV disease progression occurs over a period of 20 to 30 years, with the majority of HCV-infected individuals generally exhibiting no major symptoms in the early stages of the disease. Therefore, until a major symptom is diagnosed, many individuals are unaware they are infected and live undiagnosed without seeking treatment. For that reason, combined with the new availability of effective treatments for HCV, the United States Centers for Disease Control and Prevention, or CDC, issued new guidelines in 2013 recommending screening for all Americans born between the years 1945 and 1965 so that HCV-infected individuals will be aware of their condition and can consider treatment options.

An estimated 58 million people worldwide are chronically infected with HCV and have an increased risk of eventually developing liver cirrhosis or liver cancer. Approximately 290,000 people die every year from HCV-related liver diseases. According to the CDC, the incidence rate of acute HCV has increased 15% since 2019, with an estimated 66,700 new infections in 2020, the most recent year for which the CDC has published data. During 2020, 41 states reported a total of 107,300 newly identified chronic HCV cases in 2020, corresponding to 40.7 chronic HCV cases per 100,000. HCV-associated deaths during 2020 increased 4% (3.45 deaths per 100,000 people), compared to 2019 (3.33 deaths per 100,000 people). We believe that the chronically infected population remains significantly untreated, even with the introduction of several new treatment regimens beginning in 2013.

The approved treatments for HCV have provided significant benefit to HCV patients. To date, these treatments have cure rates approaching 100% in several subpopulations. Medical practice defines a "cure" as the point at which there is no quantifiable virus in a patient's blood for a sustained period of time after cessation of therapy, which is often referred to as a sustained virologic response, or SVR. For AbbVie's MAVYRET/MAVIRET regimen, the majority of chronic HCV patients only require 8 weeks of treatment compared to 12 weeks with other HCV regimens, including Gilead's EPCLUSA® and HARVONI® in almost all HCV genotypes.

Since the introduction of Gilead's Harvoni® and AbbVie's VIEKIRA PAK® in late 2014, the reported worldwide sales of the leading HCV therapies have declined from \$23 billion in 2015 to \$3.6 billion in 2021. Through the first nine months of calendar 2022, reported worldwide net sales were \$2.5 billion. HCV sales have declined since their peak in 2015 due to payers obtaining additional discounts, competitive market dynamics and a decline in the number of patients treated annually after the initial wave of diagnosed chronic HCV patients who had urgency for treatment. Despite the high numbers of HCV patients that have been successfully treated, there remains a large population of chronic HCV-infected patients who have yet to be treated with one of the newer "high cure" regimens. In addition, and as noted above, new HCV infections (principally in association with IV drug use) are an ongoing target population for treatment.

COVID-19 has also impacted new HCV patient volumes, HCV diagnoses, HCV prescriptions and sales of MAVYRET/MAVIRET worldwide. While new HCV infections are continuing, at this time it is uncertain when and the extent to which treatment of new HCV patients and revenues will return to pre-COVID-19 levels.

### ***Our Out-Licensed Products in AbbVie's Marketed Therapies***

**Glecaprevir** - Our protease inhibitor, glecaprevir, which is part of the latest HCV regimen from AbbVie, was developed by AbbVie in combination with pibrentasvir, AbbVie's second NS5A inhibitor. This co-formulated combination, marketed under the tradenames MAVYRET® (U.S.) and MAVIRET® (ex-U.S.), contains two novel DAAs that target and inhibit proteins essential for the replication of HCV. MAVYRET/MAVIRET is approved in the U.S., EU, Japan and numerous other countries globally as an 8-week, pan-genotypic, fixed-dose combination treatment, dosed once-daily as three oral tablets, taken with food, for chronic HCV patients without cirrhosis and new to treatment. MAVYRET/MAVIRET is also approved as a treatment for patients with specific treatment challenges, including those GT-1 patients not cured by prior treatment experience with either a protease inhibitor or an NS5A inhibitor (but not both), and in patients with limited treatment options, such as those with severe chronic kidney disease, or CKD, or those with genotype 3 chronic HCV. MAVYRET/MAVIRET is approved for use in patients across all stages of CKD with any of the major HCV genotypes (GT1-6). The approvals of MAVYRET/MAVIRET are supported by data from nine registrational studies in AbbVie's

clinical development program, which evaluated more than 2,300 patients in 27 countries across all major HCV genotypes (GT1-6) and special populations:

- **8 weeks for treatment-naïve, non-cirrhotic patients:** In November 2016, results from several Phase 3 studies of this combination demonstrated 97.5% of chronic HCV infected patients without cirrhosis and new to treatment across all major genotypes (GT1-6) achieved sustained virologic response at 12 weeks post-treatment, referred to as SVR<sub>12</sub>, with just 8 weeks of MAVYRET/MAVIRET treatment.
- **8 weeks with chronic kidney disease:** Results were also presented from AbbVie's EXPEDITION-4 study in chronic HCV patients with chronic kidney disease, or CKD, in which 98% of patients (n=102/104) across all major genotypes (GT1-6) achieved SVR<sub>12</sub> with 12 weeks of treatment with MAVYRET/MAVIRET.
- **8 weeks for GT-3:** Data from AbbVie's ENDURANCE-3 study were presented at the 2017 ILC, demonstrating that 95% of patients with challenging-to-treat, genotype 3, or GT3, chronic HCV infection, without cirrhosis and new to treatment, achieved SVR<sub>12</sub> after 8 weeks of treatment with MAVYRET/MAVIRET.
- **8 weeks for compensated cirrhosis:** Based on data from AbbVie's EXPEDITION-8 study, which demonstrated that with 8 weeks of MAVYRET treatment, 100 percent (n=273/273) of genotype 1, 2, 4, 5 and 6 patients achieved a sustained virologic response 8 weeks after treatment (SVR<sub>8</sub>) per protocol analysis. Based on this data and a second cohort of the study in GT3 chronic HCV-infected patients, MAVYRET is now approved for all genotypes with compensated cirrhosis in the U.S.

**Paritaprevir** - The first protease inhibitor developed through our collaboration with AbbVie, paritaprevir, is part of AbbVie's 3-DAA regimen approved for the treatment of genotype 1 and 4 HCV patients. This 3-DAA combination was sold as VIEKIRA PAK<sup>®</sup> (paritaprevir/ritonavir/ombitasvir/dasabuvir) in the U.S. from December 2014 to December 2018, and as VIEKIRAX<sup>®</sup>+EXVIERA<sup>®</sup> in most other jurisdictions, for non-cirrhotic patients and those with early stage, or compensated, cirrhosis. These regimens have been almost entirely replaced by MAVYRET/MAVIRET.

### Collaboration and License Agreement with AbbVie

We entered into a Collaborative Development and License Agreement with Abbott Laboratories in November 2006 to develop and commercialize HCV NS3 and NS3/4A protease inhibitors. The agreement, which was amended in January and December 2009, was then assigned to AbbVie Inc. on January 1, 2013 in connection with Abbott's transfer of its research-based pharmaceuticals business to AbbVie. Under the agreement, we have granted AbbVie an exclusive, worldwide, royalty-bearing license, including a right to grant sublicenses, to specified intellectual property, including several issued U.S. patents, relating to protease inhibitors. We also granted AbbVie access to our drug discovery capabilities in the HCV NS3 and NS3/4A protease inhibitor field. AbbVie granted us a co-exclusive (together with AbbVie), royalty-free, fully paid license, without the right to grant sublicenses, to certain of AbbVie's intellectual property, AbbVie's interest in joint intellectual property and improvements discovered by AbbVie, for the purpose of allowing us to conduct certain development and commercialization activities in the United States relating to protease inhibitors. AbbVie is responsible for and has funded all costs associated with the development, manufacturing and commercialization of paritaprevir, glecaprevir and any other compounds under this agreement. Under the agreement, we are eligible to receive milestone payments and royalties with respect to these compounds. So long as a product candidate is being developed or commercialized under the agreement, we undertake not to conduct any activity, or grant licenses to a third party, relating to protease inhibitors.

A joint steering committee was established under the agreement with review and oversight responsibilities for all research, development and commercialization activities. The joint steering committee is comprised of three of our senior personnel and three senior personnel from AbbVie; however, AbbVie has final authority to make all decisions regarding development and commercialization activities.

The research program and the evaluation period, which was performed by both parties, ended in June 2011. The first commercialized compound was paritaprevir with the second commercialized compound, glecaprevir, approved in 2017 and marketed under the tradenames MAVYRET<sup>®</sup> (U.S.) or MAVIRET<sup>™</sup> (ex-U.S.). Under this collaboration we have received \$396 million in payments from AbbVie for license payments, proceeds from a sale of preferred stock, research funding payments and milestone payments.

We also receive annually tiered, double-digit royalties per protease inhibitor product developed under the agreement, which range from ten percent up to twenty percent, or on a blended basis from the low double digits up to the high teens. However, if a product is determined to be a combination product, as is the case for both glecaprevir and paritaprevir, the net sales of the combination product are adjusted on a country-by-country and product-by-product basis to reflect a good faith determination of the relative value of each pharmaceutically active ingredient, based on the estimated fair market value. This means that a portion of AbbVie's worldwide annual net sales of a combination product or regimen is first allocated to one of our protease inhibitors and then that royalty-bearing portion is multiplied by the annually tiered royalty rates to determine our actual royalty for the protease product in that regimen in a given period. Under the terms of our agreement, as amended in October 2014, 50% of AbbVie's net sales of MAVYRET/MAVIRET are

allocated to glecaprevir. Beginning with each January 1, the cumulative net sales of a given royalty-bearing protease inhibitor product start at zero for purposes of calculating the tiered royalties on a product-by-product basis. Under this collaboration, we have received royalty payments from AbbVie totaling \$812 million through September 30, 2022. Further details of these tiered royalties are set forth in Note 7 in Notes to Consolidated Financial Statements included in this report, which are incorporated herein by this reference.

Royalties owed to us under the agreement can be reduced by AbbVie in certain circumstances, including (i) if AbbVie exercises its right to license or otherwise acquire rights to intellectual property controlled by a third party where a product could not be legally developed or commercialized in a country without the third-party intellectual property right, (ii) where a product developed under the collaboration agreement is sold in a country and not covered by a valid patent claim in such country, or (iii) where sales of a generic product are equal to at least a specified percentage of AbbVie's market share of a product in a country.

AbbVie's obligation to pay royalties on products developed under the agreement expires on a country-by-country and product-by-product basis upon the later of (i) the date of expiration of the last of the licensed patents with a valid claim covering the product in the applicable country, and (ii) ten years after the first commercial sale of the product in the applicable country.

Our intellectual property existing as of the effective date of the agreement remains our property. Any intellectual property jointly developed is jointly owned. We will have the unilateral right to enforce our patent rights on any covered product following the first commercial sale of such product, as will AbbVie. In the event of infringement related to any of our patents, we will have the first right and option to initiate legal proceedings or take other actions. In the event of infringement related to any AbbVie patents, AbbVie will have the first right and option to initiate legal proceedings or take other actions. In the event of infringement of a joint patent right, we will discuss with AbbVie whether to initiate legal proceedings or take other actions. AbbVie will have the obligation to defend at its sole expense any actions brought against either party alleging infringement of third-party rights by reason of the activities conducted under the agreement and we will have the right to obtain separate counsel at our own expense. Additionally, AbbVie, at its sole expense, will be responsible for all trademark prosecution.

Subject to the exceptions described above, a party's rights and obligations under the agreement continue until: (i) such time as AbbVie is no longer developing a product candidate or (ii) if, as of the time AbbVie is no longer developing any product candidates, AbbVie is commercializing any other protease inhibitor product, such time as all royalty terms for all covered products and all co-development terms for all co-developed products have ended. Accordingly, the final expiration date of the agreement is currently indeterminable.

Either party may terminate the agreement for cause in the event of a material breach, subject to prior notice and the opportunity to cure, or in the event of the other party's bankruptcy. Additionally, AbbVie may terminate the agreement for any reason upon specified prior notice.

If we terminate the agreement for cause or AbbVie terminates without cause, any licenses and other rights granted to AbbVie will terminate and AbbVie will be deemed to have granted us (i) a non-exclusive, perpetual, fully paid, worldwide, royalty-free license, with the right to sublicense, under AbbVie's intellectual property used in any product candidate and (ii) an exclusive (even as to AbbVie), perpetual, fully paid, worldwide, royalty-free license, with the right to sublicense, under AbbVie's interest in joint intellectual property rights to develop product candidates resulting from covered compounds and to commercialize any products derived from such compounds. Upon our request, AbbVie will also transfer to us all right, title and interest in any related product trademarks, regulatory filings and clinical trials.

If AbbVie terminates the agreement for our uncured breach, the royalty payments payable by AbbVie may be reduced, the licenses granted to AbbVie will remain in place, we will be deemed to have granted AbbVie an exclusive license under our interest in joint intellectual property, AbbVie will continue to have the right to commercialize any covered products, and all rights and licenses granted to us by AbbVie will terminate.

## **Drug Discovery**

We have internally discovered all of the compounds in our research and development programs. Our scientists have expertise in the areas of medicinal chemistry, molecular virology, pharmacology, and toxicology with highly developed sets of skills in compound generation, target selection, screening and pharmacology, preclinical development and lead optimization. We are utilizing these skills and capabilities in our discovery and development of virology and liver disease product candidates.

We focus on virology and other disease indications representing large and growing market opportunities with significant unmet medical needs. Our selection of a particular therapeutic target within those disease indications takes into consideration the experience and expertise of our scientific team and includes our ability to generate robust medicinal chemistry structure-activity relationships to assist lead optimization and secure relevant intellectual property rights. Once we have identified lead compounds, they are tested using *in vitro* and *in vivo* pharmacology studies and *in vivo* research models of antiviral or antibacterial efficacy.

## Business Development

We also regularly examine opportunities to in-license compounds and technologies to complement our existing internal discovery programs. In addition, we engage from time to time in discussions with third parties to out-license intellectual property that no longer fits in our strategic priorities for our internal research and development programs.

## Competition

We are engaged in segments of the pharmaceutical industry that are highly competitive and rapidly changing. Many large pharmaceutical and biotechnology companies, academic institutions, governmental agencies and other public and private research organizations are commercializing or pursuing the development of products that target HCV, RSV, SARS-CoV-2, HBV, hMPV and other viral infections or other diseases that we may target in the future.

Many of our competitors have substantially greater commercial infrastructures and financial, technical and personnel resources than we have, as well as drug candidates in late-stage clinical development. We will not be able to compete successfully unless we are able to:

- design and develop products that are superior to other products in the market;
- attract qualified scientific, medical, regulatory, sales and marketing and commercial personnel;
- obtain patent and/or other proprietary protection for our processes and product candidates;
- obtain required regulatory approvals; or
- collaborate with others in the development and commercialization of new products.

Established competitors may invest heavily to quickly discover and develop novel compounds that could make our product candidates obsolete. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety, or some combination of these factors, to overcome competition and to be commercially successful.

We expect AbbVie's MAVYRET/MAVIRET to continue to face intense competition due to existing approved products in the HCV market. AbbVie's MAVYRET/MAVIRET regimen currently faces competition in various world markets and subpopulations of HCV from Gilead's Epclusa® (a fixed dose combination of sofosbuvir and velpatasvir), Vosevi® (a triple combination therapy of sofosbuvir, velpatasvir and voxilaprevir approved by the FDA for specified sofosbuvir -treatment failures and NS5A-inhibitor treatment failures) and Harvoni® (a fixed-dose combination of sofosbuvir and ledipasvir); and to a lesser extent - Merck's Zepatier® (a fixed-dose combination of grazoprevir and elbasvir). Gilead launched authorized generic versions of Epclusa and Harvoni through its subsidiary, Asegua Therapeutics, LLC, which have had an impact on the competitive landscape. For example, the state of Louisiana selected Asegua as their HCV subscription model pharmaceutical partner to provide the state with unrestricted access to its direct-acting antiviral medication.

Other competitive products in the form of other treatment methods or a vaccine for HCV may render MAVYRET/MAVIRET obsolete or noncompetitive. MAVYRET/MAVIRET will face competition based on its safety and effectiveness, reimbursement coverage, price, patent position, AbbVie's marketing and sales capabilities, and other factors. If MAVYRET/MAVIRET faces competition from generic products other than authorized generic versions by the manufacturer of the branded product (i.e. Gilead and Asegua Therapeutics), our collaboration agreement provides that the royalty rate applicable to our protease product contained in the regimen is reduced significantly by a specified percentage on a product-by-product, country-by-country basis. If AbbVie is not able to compete effectively against its competitors in HCV, our business will not grow and our financial condition, operations and stock price will suffer.

Similarly, RSV, COVID-19 and HBV represent competitive therapeutic areas. For RSV, there are currently no safe and effective therapies for already established RSV infection. Several companies are seeking to develop new antiviral treatments for RSV infection in adult and pediatric patients. Ark Biosciences, Pfizer/ReViral (acquired in June 2022) and Merck all have compounds in clinical development. Synagis, a prophylactic, monoclonal-antibody-based treatment from AstraZeneca, which is commercialized by AbbVie outside the U.S., is approved for infants considered at high risk for RSV infection; however, studies have found that most young children with RSV infection were previously healthy, and thus would not normally be prescribed prophylactic treatment. AstraZeneca/Sanofi and Merck are developing long-acting versions of the monoclonal antibody for prophylaxis use in infants. In addition, a number of companies have RSV vaccines in development, primarily directed at prevention of RSV infection, and some companies are also evaluating vaccines in a therapeutic mode for treatment of established RSV infection.

Currently, there are two Emergency Use Authorizations of oral antiviral treatments for non-hospitalized, high-risk patients with SARS-CoV-2 infection: Paxlovid, a 3CL protease inhibitor, and Molnupiravir, a polymerase inhibitor. Additionally, there are companies developing oral direct acting antivirals for SARS-CoV-2 that are currently in Phase 2 or 3 studies including Shionogi, Toyama, Atea, Pardes, SyneuRx and Todos as well as additional compounds in Phase 1 studies.



While there are antiviral medications prescribed for HBV that can suppress HBV DNA, they generally have low cure rates, resulting in the need for lifelong treatment. Many companies are seeking to develop new HBV drugs, including GIB, Gilead, Green Cross, GSK/Ionis, HEC Pharma, Johnson & Johnson/Janssen, Qilu, Replicor, Roche, Vaccitech, VBI Vaccines and Vir Biotechnology, which have Phase 2 programs in progress, with many of these companies conducting earlier stage programs as well. In addition, a number of companies have Phase 1 or earlier stage HBV programs.

If we are not able to develop new products that can compete effectively against our current and future competitors, our business will not grow and our financial condition, operations and stock price will suffer.

## Intellectual Property

As part of our business strategy, we actively seek patent protection for our product candidates in the United States and certain major foreign jurisdictions and file additional patent applications, when appropriate, to cover improvements to our compounds. We also rely on trade secrets, internal know-how, technological innovations and agreements with third parties to develop, maintain and protect our competitive position. Our ability to be competitive will depend on the success of this strategy.

Each of our major research and development programs, including RSV, SARS-CoV-2, HBV and hMPV, as well as our out-licensed products for HCV and our FXR agonist assets, typically has several pending patent claims and issued patents in the program area containing claims to compounds, methods of use and processes for synthesis. However, only a few of the issued patents and/or pending patent applications cover the lead product candidate in a given program.

*RSV, SARS-CoV-2, HBV.* Our patent portfolio directed to N- and L-protein inhibitors for RSV, protease inhibitors for SARS-CoV-2 and core inhibitors for HBV, includes issued U.S. patents or pending U.S. patent applications, or both, as well as numerous foreign patent applications. We expect that our existing patents and patent applications (assuming patents are ultimately issued), will provide patent coverage in the U.S., if and when a compound is approved by the FDA, until at least 2038 for each of our compounds currently in clinical development.

*HCV NS3 Protease Inhibitor Program.* The patent portfolio directed to the HCV protease inhibitor program with AbbVie includes U.S. patents and foreign patents, as well as non-provisional applications. The issued U.S. composition-of-matter patent covering paritaprevir is expected to expire in 2031. The issued U.S. composition-of-matter patent covering glecaprevir is expected to expire in 2032. AbbVie is a joint owner of a number of the non-provisional patent applications. AbbVie also has rights to some or all of these patents and patent applications pursuant to its collaboration agreement with us.

We may obtain patents for certain compounds many years before we obtain marketing approval for products containing such compounds. Because patents have a limited life, which usually begins to run well before the first commercial sale of the related product, the commercial value of the patent may be limited. However, we may be able to apply for patent term extensions in the United States and in a number of European countries, compensating in part for delays in obtaining marketing approval, but we cannot be certain we will obtain such extensions.

It is also very important that we do not infringe patents or other proprietary rights of others. If we do infringe such patents or other proprietary rights, we could be prevented from developing or selling products or from using the processes covered by those patents, could be required to pay substantial damages, or could be required to obtain a license from the third party to allow us to use their technology, which may not be available on commercially reasonable terms or at all. If we were not able to obtain a required license or develop alternative technologies, we may be unable to develop or commercialize some or all of our products, and our business could be adversely affected.

In addition, we jointly own patent applications, together with AbbVie, that claim paritaprevir and glecaprevir as a chemical entity. However, there is no guarantee that such applications will issue. Further, the existence of issued patents does not guarantee our right to practice the patented technology or commercialize the patented product. Third parties may have already or could obtain rights to patents that could be used to prevent or attempt to prevent us from commercializing our product candidates. If these other parties are successful in obtaining valid and enforceable patents, and establishing our infringement of those patents, we could be prevented from commercializing our product candidates unless we were able to obtain a license under such patents, which may not be available on commercially reasonable terms or at all.

Much of our scientific capabilities depend upon the knowledge, experience and skills of key scientific and technical personnel. To protect our rights to our proprietary know-how and technology, we endeavor to require all employees, as well as our consultants and advisors, when feasible, to enter into confidentiality agreements that require disclosure and assignment to us of ideas, developments, discoveries and inventions made by these employees, consultants and advisors in the course of their service to us.

We may be unable to obtain, maintain and protect the intellectual property rights necessary to conduct our business, and we may be subject to claims that we infringe or otherwise violate the intellectual property rights of others, which could materially harm our business. For more information, see “Risk Factors—Risks Related to Our Intellectual Property Rights.”

## Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of products such as those we develop. Any pharmaceutical candidate that we develop must be approved by the FDA before it may be legally marketed in the United States and by the appropriate foreign regulatory agency before it may be legally marketed in foreign countries.

### *United States Drug Development Process*

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act, or FDCA, and implementing regulations. Drugs are also subject to other federal, state and local statutes and 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. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

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

- Completion of preclinical laboratory tests, animal studies and formulation studies according to Good Laboratory Practice, or GLPs, or other applicable regulations;
- Submission to the FDA of an Investigational New Drug Application, or an IND, which must become effective before human clinical trials may begin;
- Performance of adequate and well-controlled human clinical trials according to the FDA's current Good Clinical Practice, or GCPs, to establish the safety and efficacy of the proposed drug for its intended use;
- Submission to the FDA of a New Drug Application, or an NDA, for a new drug product;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the drug is to be produced to assess compliance with the FDA's current Good Manufacturing Practice standards, or cGMP, to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- Potential FDA audit of the nonclinical and clinical trial sites that generated the data in support of the NDA; and
- FDA review and approval of the NDA.

The lengthy process of seeking required approvals, which can often take anywhere from six months from the time the NDA is filed if there is a priority review for a breakthrough therapy to at least twelve months for a standard review, and the continuing need for compliance with applicable statutes and regulations require the expenditure of substantial resources. There can be no certainty that approvals will be granted.

Before testing any compounds with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with GLP and other federal regulations and requirements. The sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug at any time before or during clinical trials due to safety concerns or non-compliance. Accordingly, we cannot assure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that result in suspension or termination of such trial.

Clinical trials involve the administration of the product candidate to healthy volunteers or patients having the disease being studied under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety. Each protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted in accordance with the FDA's GCP requirements. Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits.

The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until it is completed.

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

- *Phase 1.* The drug is initially introduced into healthy humans and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted only in patients having the specific disease.
- *Phase 2.* The drug is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule for patients having the specific disease.
- *Phase 3.* Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials, which usually involve more patients than earlier trials, are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling. Generally, at least two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA.

Post-approval studies, or Phase 4 clinical trials, may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and may be required by the FDA as part of the approval process.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA by the investigators for serious and unexpected adverse events or any finding from tests in laboratory animals that suggests a significant risk for human patients. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA, or the sponsor or its data safety monitoring board, may suspend a clinical trial at any time on various grounds, including a finding that the research 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 drug has been associated with unexpected serious harm to patients.

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

### ***U.S. Review and Approval Processes***

The results of product development, preclinical 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 by the applicant; a waiver of such fees may be obtained under certain limited circumstances.

In addition, under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers.

The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA has twelve months in which to complete its initial review of a standard NDA and respond to the applicant, and six months for a priority NDA. The review clock for an NDA may be extended if a major amendment is submitted during the review cycle. In addition, the FDA does not always meet its PDUFA goal dates for standard and priority NDAs.

After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. In addition to its own review, the FDA may refer applications for novel drug products or drug products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and 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. During the approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy, or REMS, is necessary to assure the safe use of the drug. If the FDA concludes that a REMS is needed, the sponsor of the NDA must submit a proposed REMS; the FDA will not approve the NDA without a REMS, if required.

Before approving an NDA, the FDA will inspect the facilities at which the product is to be manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information.

The NDA review and approval process is lengthy and difficult, and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA will issue a “complete response” letter if the agency decides not to approve the NDA. The complete response letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may require Phase 4 testing, which involves clinical trials designed to further assess a product’s safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized.

### ***Expedited Development and Review Programs***

The FDA has four programs intended to expedite the development and review of new drugs addressing unmet medical needs or treating serious or life-threatening conditions: fast track, breakthrough therapy, priority review, and accelerated approval, in addition to emergency use authorization, or EUA, in situations such as the COVID-19 pandemic.

The FDA “fast track” program is intended to expedite or facilitate the process for reviewing new products to treat serious or life-threatening conditions and address unmet medical needs. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. Under the fast track program, the sponsor will have more frequent interactions with the FDA during drug development, and may also submit sections of the NDA on a rolling basis to the FDA for review before submitting the complete application. Fast track does not guarantee that a product will be reviewed more quickly or receive FDA approval.

The FDA “breakthrough therapy” program is intended to expedite the development and review of drugs for serious or life-threatening conditions. Preliminary clinical evidence must show that the drug may have substantial improvement over existing therapies on one or more clinically significant endpoints. Although the drug does not have to address an unmet medical need, designation of breakthrough therapy status carries all the “fast track” program features. Additionally, the breakthrough therapy program entitles the sponsor to earlier and more frequent interaction with the FDA review team regarding development of nonclinical and clinical data, and allows the FDA to offer product development and regulatory advice necessary to shorten the time for product approval. The breakthrough therapy status does not guarantee a quicker development or review of the product, and does not ensure FDA approval.

The FDA also has a “priority review” program for products offering significant improvement in the treatment, diagnosis or prevention of a disease. The goal of the priority review program is to shorten the review period to six months from the twelve months required for standard review. Any drug with breakthrough therapy, accelerated approval designation, or fast track can be granted priority review if it meets the necessary criteria.

The FDA “accelerated approval” program is intended to expedite the development and review of products with the potential to treat serious or life-threatening illnesses and provide meaningful therapeutic benefit over existing treatments. The program allows approval of a product on the basis of adequate and well-controlled clinical studies establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint that can be measured earlier than survival or irreversible morbidity. As a condition of approval, the FDA generally requires that a sponsor of the product perform adequate and well-controlled post-marketing clinical studies to establish safety and efficacy for the approved indication. Failure to conduct such studies or failure of the studies to establish required safety and efficacy may result in revocation of approval. The FDA also requires, as a condition for accelerated approval, pre-approval of promotional materials, which could adversely impact the timing of the commercial launch or subsequent marketing of the product.



The FDA may also allow the use of unapproved medical products, or unapproved uses of approved medical products, under an emergency use authorization, or EUA, to diagnose, treat, or prevent serious or life-threatening diseases or conditions when certain statutory criteria have been met, including that there are no adequate, approved, and available alternatives. An EUA is a mechanism to facilitate the availability and use of medical countermeasures during public health emergencies, such as the COVID-19 pandemic. Once submitted, the FDA will evaluate an EUA request and determine whether the relevant statutory criteria are met, taking into account the totality of the scientific evidence about the drug that is available to FDA. EUAs can be terminated, revoked or reissued, depending on the state of the public health emergency and new data about the drug.

### ***Post-Approval Requirements***

Any drug products for which we receive FDA approvals are subject to continuing regulation by the FDA. Certain requirements include, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information on an annual basis or more frequently for specific events, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements. These promotion and advertising requirements include, among others, standards for direct-to-consumer advertising, prohibitions against promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use"), rules for conducting industry-sponsored scientific and educational activities and promotional activities involving the internet. Failure to comply with FDA requirements can have negative consequences, including the immediate discontinuation of noncomplying materials, adverse publicity, enforcement letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our product candidates. Manufacturers of our product candidates are required to comply with applicable FDA manufacturing requirements contained in the FDA's cGMP regulations. These regulations require, among other things, quality control and quality assurance as well as the corresponding maintenance of comprehensive records and documentation. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are also required to register their establishments and list any products they make with the FDA and to comply with related requirements in certain states. These entities are further subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in serious and extensive restrictions on a product, manufacturer or holder of an approved NDA. These restrictions may include suspension of a product until the FDA is assured that quality standards can be met, continuing oversight of manufacturing by the FDA under a "consent decree," which frequently includes the imposition of costs and continuing inspections over a period of many years, as well as possible withdrawal of the product from the market. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented. Other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

The FDA also may require post-marketing testing, known as Phase 4 testing, as well as risk minimization action plans and surveillance to monitor the effects of an approved product or place conditions on an approval that could otherwise restrict the distribution or use of the product.

### ***U.S. Patent Term Restoration and Marketing Exclusivity***

#### ***Drug Price Competition and Patent Term Restoration Act of 1984***

Depending upon the timing, duration and specifics of the FDA approval of the use of our product candidates, some of our United States patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during federal regulatory review preceding the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted within 60 days of approval, prior to the expiration of the patent. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA. However, there is no guarantee that any such application will be approved.

### *Federal Food, Drug and Cosmetic Act, or FDCA*

Market exclusivity provisions under the FDCA, which are independent of patent status and any patent related extensions, can also delay the submission or the approval of certain applications of other companies seeking to reference another company's NDA. If the new drug is a new chemical entity subject to an NDA, the FDCA provides a five-year period of non-patent marketing exclusivity within the United States 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 functional group of a molecule responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a so-called Section 505(b)(2) NDA, submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, such 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 also 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 conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. 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 all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

### ***Other U.S. Healthcare Laws and Compliance Requirements***

In the United States, our activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare and Medicaid Services (formerly the Health Care Financing Administration), other divisions of the United States Department of Health and Human Services (e.g., the Office of Inspector General), the United States Department of Justice and individual United States Attorney offices within the Department of Justice, state attorney generals and state and local governments. For example, sales, marketing and scientific/educational grant programs must comply with the anti-fraud and abuse provisions of the Social Security Act, the False Claims Act, the privacy and security provisions of the Health Insurance Portability and Accountability Act, or HIPAA, and similar state laws, each as amended. Pricing and rebate programs must comply with the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990 and the Veterans Health Care Act of 1992, each as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Under the Veterans Health Care Act, or VHCA, drug companies are required to offer certain pharmaceutical products at a reduced price to a number of federal agencies including the United States Department of Veterans Affairs and United States Department of Defense, the Public Health Service and certain private Public Health Service—designated entities in order to participate in other federal funding programs including Medicare and Medicaid. Recent legislative changes purport to require that discounted prices be offered for certain United States Department of Defense purchases for its TRICARE program via a rebate system. Participation under the VHCA requires submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, as well as the entry into government procurement contracts governed by the Federal Acquisition Regulations.

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of pharmaceutical products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

### ***Europe / Rest of World Government Regulation***

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products.

Whether or not we obtain FDA approval for a product, 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. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the European Union, for example, a clinical trial application, or CTA, must be submitted to

each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical trials may proceed.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with International Conference on Harmonisation (ICH) / WHO Good Clinical Practice standards and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational drug under European Union regulatory systems, we must submit a marketing authorization application to the European Medicines Agency, or the EMA. The application used to file an NDA in the United States is similar to that required in the European Union, with the exception of, among other things, country-specific document requirements.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials are conducted in accordance with GCPs and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

### ***Pharmaceutical Coverage, Pricing and Reimbursement***

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of reimbursement from third-party payors. Third-party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the drug product. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drug products for a particular indication. 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. We may need to conduct expensive pharmaco-economic studies to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Our product candidates may not be considered medically necessary or cost-effective. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

In 2003, the United States government enacted legislation providing a partial prescription drug benefit for Medicare recipients, which became effective at the beginning of 2006. Government payment for some of the costs of prescription drugs may increase demand for any products for which we receive marketing approval. However, to obtain payments under this program, we would be required to sell products to Medicare recipients through private prescription drug plans that contract with the federal government and adhere to certain minimum requirements.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively known as the Affordable Care Act, or ACA, substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the pharmaceutical industry.

The comprehensive overhaul extended coverage to approximately 20 million previously uninsured Americans. Since its adoption, the ACA contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse, which have affected existing government healthcare programs and have resulted in the development of new programs, including Medicare payment tied to performance. Additionally, the Affordable Care Act:

- 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, under which they must agree to offer 50% 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, beginning January 2011; and
- imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs" to specified federal government programs.

Several states have not implemented the provisions of the ACA that involve the expansion of Medicaid eligibility to low-income adults. While the United States Supreme Court recently rejected the latest challenge to the constitutionality of the ACA, it is possible

that other legislative efforts may seek to modify it. In addition, other legislative changes have been proposed since the Affordable Care Act was enacted.

There has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. For example, the Inflation Reduction Act of 2022, or IRA, introduces some of the most significant changes to Medicare payment for prescription drugs since the ACA. Among its many provisions, the IRA authorizes the Medicare program to negotiate pricing for certain high-cost drugs, including physician-administered and self-administered drugs, that have been on the market for a minimum amount of time without generic competition. Each year, beginning with calendar year 2026, the Secretary of the Department of Health and Human Services will implement a negotiated price, known as the “Maximum Fair Price”, or MFP, that will be made public and apply to the drug’s Medicare utilization if the drug is among the top 10 drugs with the highest Medicare spending. Manufacturers who fail to offer the MFP, or fail to come to the table to negotiate after the Secretary has determined their drug is eligible for negotiation, will incur an excise tax of up to 95% for each sale of the drug in the United States. Depending on the share of Medicare spending each year that is attributed to MAVYRET or any other drug we may develop or out-license, and whether or not those drugs become eligible for Medicare negotiation, those drugs and our revenue may be adversely impacted by this provision.

The IRA also will require manufacturers, beginning in 2023, to rebate the Medicare program for Medicare utilization of drugs that have price increases faster than the rate of inflation. The benchmark to which price increases are compared will vary depending on the drug. Although manufacturers are generally familiar with inflation rebates under the Medicaid program, where they have existed for decades, the IRA represents the first time that the Centers for Medicare and Medicaid Services, or CMS, has extended inflation rebates to the Medicare program.

The IRA also redesigns the Medicare prescription drug benefit in several important ways, beginning in calendar year 2025. First, the IRA places an annual out-of-pocket cap on Medicare beneficiary cost sharing amounts, which will actually take effect in calendar year 2024 before the full benefit redesign. Previously, beneficiaries’ out-of-pocket costs were uncapped, even if heavily subsidized. Second, the IRA requires that manufacturers share in the cost of prescription drugs throughout the prescription drug benefit. Previously manufacturers only needed to offer discounted pricing for a single phase of the prescription drug benefit. Finally, the IRA shifts the majority of liability in the “catastrophic phase”—the phase of the prescription drug benefit that only the costliest of Medicare beneficiaries enter—to the private Part D plans, thereby encouraging them to better manage costs. Previously, the Federal government incurred the vast majority of liability during the catastrophic phase. Together, these changes to the Medicare prescription drug benefit will create new pricing dynamics for payers and manufacturers.

Different pricing and reimbursement schemes exist in other countries. In the European Union, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any drug candidates for which we receive regulatory approval for commercial sale may suffer if the government and third-party payers fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on pharmaceutical drug pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

## **Research and Development**

Our research and development expenses were \$164.5 million, \$174.1 million and \$136.8 million for the fiscal years ended September 30, 2022, 2021, and 2020, respectively.

## **Manufacturing**

We do not have our own manufacturing capabilities, except with respect to limited amounts of active pharmaceutical ingredients needed for preclinical development. To date, we have relied on third-party manufacturers, including manufacturers in China, for supply of active pharmaceutical ingredients and ingredients for use in clinical trials of our product candidates. We also expect that in the future we will rely on such manufacturers to produce commercial quantities of any product candidates that we commercialize ourselves. Manufacturing for gileadprevir is conducted by AbbVie. Wherever possible, we seek to identify multiple suppliers for raw materials and key intermediaries to be used in our manufacturing process.



## **Sales and Marketing**

We currently do not have any commercialization or sales and marketing capabilities, and currently have no fixed plans to invest in or build such capabilities internally. We have partnered our protease inhibitor compounds for HCV with AbbVie. We may also partner or collaborate with, or license commercial rights to, other larger pharmaceutical or biopharmaceutical companies to support the development of one or more of our wholly-owned product candidates through late-stage clinical development and, if successful, commercialization. However, we still retain all commercial rights to our independent programs and we will continue to evaluate our alternatives for commercializing them once they are more advanced in their clinical development.

## **Our Corporate Information**

We are a Delaware corporation, incorporated in 1995. Our principal executive offices are located at 500 Arsenal Street, Watertown, Massachusetts 02472, and our telephone number is (617) 607-0800. Our web site address is <http://www.enanta.com>.

## **Segment Information**

We provide segment information in Note 2 to our Consolidated Financial Statements included in Item 8 of this report. We are incorporating that information into this section by this reference.

## **Human Capital Resources**

As of September 30, 2022, we had 160 full-time employees, 74 of whom hold Ph.D. or M.D. degrees and an additional 40 of whom hold a master's degree or other post-graduate degree. We consider the intellectual capital of our employees to be an essential driver of our business and key to our future prospects. Historically we have had relatively low turnover of employees, but as our headcount has grown in the past three years and the number of biotechnology and pharmaceutical companies in the Boston area has increased dramatically, we have experienced an increase in the number of employees leaving for other opportunities. Given our financial resources and our track record, we continue to be able to fill the vacated positions and grow our headcount in support of our expanding pipeline of research programs and product candidates. We also monitor our compensation programs closely and provide what we consider to be a very competitive mix of compensation and insurance benefits for all our employees, as well as participation in our equity programs. None of our employees is subject to a collective bargaining agreement or represented by a trade or labor union. We consider our relations with our employees to be good.

## **Available Information**

Our Internet website address is <http://www.enanta.com>. Through our website, we make available, free of charge, our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and any amendments to those reports, as well as proxy statements, and, from time to time, other documents as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission, or SEC. These SEC reports can be accessed through the “Investors” section of our website. The information found on our website is not part of this or any other report we file with or furnish to the SEC.

In addition, the SEC maintains an Internet website that contains reports, proxy and information statements, and other information regarding Enanta Pharmaceuticals, Inc. and other issuers that file electronically with the SEC. The SEC’s Internet website address is <http://www.sec.gov>.

## ITEM 1A. RISK FACTORS

### RISK FACTORS

Our business faces significant risks and uncertainties. Certain factors may have a material adverse effect on our business prospects, financial condition and results of operations, and you should carefully consider them. Accordingly, in evaluating our business, we encourage you to consider the following discussion of risk factors, in its entirety, in addition to other information contained in or incorporated by reference into this Annual Report on Form 10-K and our other public filings with the SEC. Other events that we do not currently anticipate or that we currently deem immaterial may also affect our business, prospects, financial condition and results of operations.

#### Risks Related to Our Business

***Our financial prospects for the next several years are dependent upon AbbVie's success selling MAVYRET/MAVIRET, which includes our protease inhibitor, glecaprevir, for the treatment of HCV. AbbVie may continue to experience lower sales volume in future quarters due to a reduction in diagnoses and treatment of HCV, which could adversely affect our business.***

We rely on AbbVie to commercialize its regimen containing glecaprevir (our second protease inhibitor, which is one of the two DAAs in AbbVie's MAVYRET/MAVIRET treatment), over which we have granted AbbVie complete control. Our ability to continue to generate revenue in the short term will depend primarily on the success of AbbVie's efforts to maintain sales of MAVYRET/MAVIRET. Such success is subject to uncertainty, and we have no control over the resources, time and effort that AbbVie may devote to sales of this regimen. Any of several events or factors could have a material adverse effect on our ability to continue to generate revenue from AbbVie's sales of MAVYRET/MAVIRET. For example, AbbVie:

- may continue to experience lower sales volume in future quarters due to a reduction in diagnoses and treatment of HCV if doctor visits and other routine healthcare activities remain at below normal levels as a result of the COVID-19 pandemic;
- may not maintain satisfactory levels of prescriptions by physicians and reimbursement by third-party payors for the MAVYRET/MAVIRET regimen in the various markets of the world where it is being sold;
- may not compete successfully with its MAVYRET/MAVIRET regimen against other products and therapies for HCV, including competition for exclusive arrangements with third-party payors and governmental entities as well as price competition;
- may have to comply with additional requests and recommendations from the FDA, including label restrictions for its regimen containing glecaprevir;
- may not obtain all commercially necessary reimbursement approvals;
- may not commit sufficient resources to the marketing and distribution of MAVYRET/MAVIRET, whether for competitive or strategic reasons or otherwise due to a change in business priorities;
- may cease to perform its obligations under the terms of our collaboration agreement; and
- may unilaterally terminate our collaboration agreement on specified prior notice without any reason and without any further commitment.

We do not have access to all information regarding AbbVie's MAVYRET/MAVIRET, including certain information about spontaneous safety reports for any marketed product, regulatory affairs, process development, manufacturing, marketing, sales and other areas known by AbbVie. Thus, our ability to keep our stockholders informed about the status of the marketed products licensed under our collaboration is limited by the degree to which AbbVie keeps us informed. If AbbVie does not perform in the manner we expect or fulfill its responsibilities in a timely manner, or at all, the global commercialization of MAVYRET/MAVIRET could be terminated in selected jurisdictions or be commercially unsuccessful. In addition, AbbVie has the right to make decisions regarding the commercialization of licensed products without consulting us. For example, in 2018 AbbVie entered into a royalty-free licensing agreement with the Medicines Patent Pool to accelerate access to generic versions of MAVYRET/MAVIRET in 99 low- and middle-income countries and territories. AbbVie may also make decisions with which we do not agree. If AbbVie acts in a manner that is not in our best interest, then it could adversely affect our business and prospects.

***Our royalty revenues are derived from AbbVie's net sales of its MAVYRET/MAVIRET regimen for HCV. If AbbVie is unable to maintain sales of this regimen at or above current levels of sales, our royalty revenues will be adversely affected.***

AbbVie's MAVYRET/MAVIRET regimen continues to be the leading HCV treatment in the U.S. and several market geographies in developed countries where it is approved. While commercialization of this regimen is exclusively in AbbVie's control without any

required input from us, we believe it is possible that prices will decline further due to payors obtaining additional discounts or competitive market dynamics. For example, the states of Louisiana and Washington have negotiated a blanket price for one of the HCV drug companies to treat all patients in one or more state programs (e.g. Medicaid). Gilead has been awarded the contract in Louisiana and other states and AbbVie has been awarded the contract in Washington and other states. In addition, Gilead has been able to access the Medicaid market at a lower price point to build its market share by using an authorized generic version of its HCV regimen branded as Epclusa®. It is unknown whether these programs or other programs that states may adopt could have any further impact on MAVYRET/MAVIRET sales. There may also be fluctuations in AbbVie's market share over time due to these and other competitive actions by Gilead.

In addition, in light of continued fiscal crises experienced by several countries in the European Union and Japan, governments have announced or implemented measures to manage and reduce healthcare expenditures. AbbVie may experience global pricing pressure for its MAVYRET/MAVIRET regimen from such measures, which may be reflected in larger discounts or rebates on its regimens or delayed reimbursement. Also, private and public payors may choose to exclude AbbVie's MAVYRET/MAVIRET regimen from their formulary coverage lists or limit the types of patients for whom coverage will be provided. Any such change in formulary coverage, discounts or rebates or reimbursement for MAVYRET/MAVIRET would negatively affect the demand for this regimen and our royalty revenue derived from its sales.

Furthermore, we expect that the COVID-19 pandemic will continue to adversely affect AbbVie's sales of MAVYRET/MAVIRET in the United States and the rest of the world if healthcare systems continue to experience varying levels of shut-down and diagnoses and treatment rates of HCV infections remain at below-normal levels. At this point in time we do not know the extent and duration of this adverse effect. We note, however, that the HCV patient pool will continue to carry the viral infection until treated.

***We and AbbVie face substantial competition in the markets for HCV drugs, and there are many companies developing potential therapies for RSV, SARS-CoV-2, HBV and hMPV which may result in others discovering, developing or commercializing products before we do or doing so more successfully than we do.***

The pharmaceutical and biotechnology industries are intensely competitive and rapidly changing. Many large pharmaceutical and biotechnology companies, academic institutions, governmental agencies and other public and private research organizations are commercializing or pursuing the development of products that target HCV, RSV, SARS-CoV-2, HBV and hMPV and other viral infections or diseases that we may target in the future. Many of our competitors have substantially greater commercial infrastructure and greater financial, technical and personnel resources than we have, as well as drug candidates in late-stage clinical development.

In all the disease areas currently under the focus of our research and development efforts, there are other companies with product candidates that are more advanced than ours. Our competitors may succeed in developing these product candidates or others and obtaining regulatory approval before we can do so with any of our product candidates. If we are not "first to market" with one of our product candidates in one or more of these disease indications, our competitive position could be compromised because it may be more difficult for us to obtain marketing approval for that product candidate and market acceptance of that product candidate as a follow-on competitor. In addition, any new product that competes with an approved product typically must demonstrate compelling advantages in efficacy, convenience, tolerability or safety, or some combination of these factors, to gain regulatory approvals, overcome price competition and be commercially successful.

We expect AbbVie's MAVYRET/MAVIRET to continue to face intense competition due to existing approved products in the HCV market. AbbVie's MAVYRET/MAVIRET regimen currently faces competition in various world markets and subpopulations of HCV from Gilead's Epclusa® (a fixed dose combination of sofosbuvir and velpatasvir), Vosevi® (a triple combination therapy of sofosbuvir, velpatasvir and voxilaprevir approved by the FDA for specified sofosbuvir -treatment failures and NS5A-inhibitor treatment failures) and Harvoni® (a fixed-dose combination of sofosbuvir and ledipasvir); and to a lesser extent - Merck's Zepatier® (a fixed-dose combination of grazoprevir and elbasvir). Gilead launched authorized generic versions of Epclusa and Harvoni through its subsidiary, Asegua Therapeutics, LLC, which have had an impact on the competitive landscape. For example, the state of Louisiana selected Asegua as their HCV subscription model pharmaceutical partner to provide the state with unrestricted access to its direct-acting antiviral medication.

Other competitive products in the form of other treatment methods or a vaccine for HCV may render MAVYRET/MAVIRET obsolete or noncompetitive. MAVYRET/MAVIRET will face competition based on its safety and effectiveness, reimbursement coverage, price, patent position, AbbVie's marketing and sales capabilities, and other factors. If MAVYRET/MAVIRET faces competition from generic products other than authorized generic versions by the manufacturer of the branded product (i.e. Gilead and Asegua Therapeutics), our collaboration agreement provides that the royalty rate applicable to our protease product contained in the regimen is reduced significantly by a specified percentage on a product-by-product, country-by-country basis. If AbbVie is not able to compete effectively against its competitors in HCV, our business will not grow and our financial condition, operations and stock price will suffer.

Similarly, RSV, COVID-19, HBV and hMPV, represent competitive therapeutic areas. While there are antiviral medications prescribed for HBV that can suppress HBV DNA, they generally have low cure rates, resulting in the need for lifelong treatment. Many companies are seeking to develop new HBV drugs that alone or in combination with other mechanisms could lead to a

functional cure for HBV. Altimmune, Arbutus, Ascletis, Assembly, Gilead, Green Cross, GSK/Ionis, HEC Pharma, Johnson & Johnson/Janssen, Qilu, Replicor, Roche, Vaccitech, VBI Vaccines and Vir Biotechnology have Phase 2 programs in progress, with many of these companies conducting earlier stage programs as well. In addition, a number of companies have Phase 1 or earlier stage HBV programs.

For RSV, there are currently no safe and effective therapies for already established RSV infection. Several companies are seeking to develop antiviral treatments for RSV infection in adult and pediatric patients. Ark Biosciences, Pfizer/ReViral (acquired in June 2022) and Merck all have compounds in clinical development. Synagis, a prophylactic, monoclonal-antibody-based treatment from AstraZeneca, which is commercialized by AbbVie outside the U.S., is approved for infants considered at high risk for RSV infection; however, studies have found that most young children with RSV infection were previously healthy, and thus would not normally be prescribed prophylactic treatment. AstraZeneca/Sanofi and Merck are developing long-acting versions of the monoclonal antibody for prophylaxis use in infants. In addition, a number of companies have RSV vaccines in development, primarily directed at prevention of RSV infection, and some companies are also evaluating vaccines in a therapeutic mode for treatment of established RSV infection.

Currently, there are two Emergency Use Authorizations of oral antiviral treatments for non-hospitalized, high-risk patients with SARS-CoV-2 infection: Paxlovid, a 3CL protease inhibitor, and Molnupiravir, a polymerase inhibitor. Additionally, there are companies developing oral direct acting antivirals for SARS-CoV-2 that are currently in Phase 2 or 3 studies including Shionogi, Toyama, Atea, Pardes, SyneuRx and Todos as well as additional compounds in Phase 1 studies.

If we are not able to develop new products that can compete effectively against our current and future competitors, our business will not grow and our financial condition, operations and stock price will suffer.

***We reported net losses for the fiscal years ended September 30, 2022 and 2021 primarily due to the impact of COVID-19 on our royalty revenues and increased levels of research and development expense as we progress our wholly-owned programs. Continued changes in royalty revenue earned under our AbbVie agreement or changes in the level of expenses associated with development of our product candidates, or both, may cause our results of operations to fluctuate from period to period. Any continuation of the recent trend of diminishing royalty revenue, combined with increasing research and development expenses in support of our advancing programs, will result in continued operating losses in this fiscal year and in future periods unless we develop other sources of revenue.***

As discussed above, our principal source of revenue continues to be our royalty revenue earned under the AbbVie collaboration agreement. There is uncertainty regarding this future revenue stream given the competitive nature of the market for HCV therapies, which reflects price competition, the changing nature of payer contracts of AbbVie and others, the varying rates of reimbursement in different countries and the impact of the COVID-19 pandemic on AbbVie's HCV sales. Changes in royalty revenue earned under the AbbVie collaboration agreement, including those that occur from period to period due to the annually tiered structure of our royalties, may cause our revenues and operating results to fluctuate significantly from quarter to quarter and could have an adverse effect on our stock price.

Additionally, many of the preclinical and clinical development activities required for our product candidates must be contracted out to contract research organizations, or CROs, at significant expense. We expect these expenses to increase substantially in the coming years as we advance compounds and conduct more clinical studies. However, the global impact of COVID-19 has had, and is likely to continue to have, an adverse effect on the ability of our CROs to conduct preclinical and clinical studies. At this point in time we do not know to what extent these studies will be further impacted by the pandemic. Additionally, inflation may further impact our future development expenses. Therefore, now more than ever it is difficult to accurately predict the timing and amounts of these expenses, and we expect that they will vary from quarter to quarter. In addition, the FDA or other regulatory agencies may require more preclinical or clinical testing than we originally anticipated for any of our product candidates. We may also be required to purchase expensive competitor drugs for use in our trials, either to demonstrate potential treatment combinations or as comparators to our product candidates. We also conduct clinical development activities outside the U.S. and are therefore exposed to foreign currency fluctuations for payments made to CROs in currencies other than the U.S. dollar. As a result, the expenses of our development programs and our operating results may fluctuate significantly from quarter to quarter. If combined with any continuation of the recent trend of reduced royalty revenue, such a trend would likely result in operating losses in the coming year and in future periods, unless we develop other sources of revenue.

***We will require substantial additional funding to achieve our goals. A failure to obtain this funding when needed could force us to delay, limit, reduce or terminate some or all of our product development efforts.***

We will continue to expend substantial resources discovering and developing our proprietary product candidates. These expenditures will include costs associated with research and development, preclinical manufacturing of product candidates, conducting preclinical



experiments and clinical trials and obtaining regulatory approvals, as well as commercializing any products later approved for sale. Our future capital requirements depend on many factors, including:

- the amount of royalties generated from MAVYRET/MAVIRET sales under our existing collaboration with AbbVie, including any continuing impact of the COVID-19 pandemic on the number of treated HCV patients;
- the number and characteristics of our research and development programs;
- the scope, progress, results and costs of researching and developing our existing product candidates on our own, including conducting advanced clinical trials;
- our ability to establish new collaborations, licensing or other arrangements, if any, and the financial terms of such arrangements;
- delays and additional expense in our clinical trials as a result of the COVID-19 pandemic;
- the cost of manufacturing our product candidates for clinical development and any products we successfully commercialize independently;
- opportunities to in-license or otherwise acquire new technologies, therapeutic candidates and therapies;
- costs associated with prosecuting our patent infringement suit regarding the use of a coronavirus 3CL protease inhibitor in Paxlovid, Pfizer's antiviral treatment for COVID-19;
- the timing of, and the costs involved in, obtaining regulatory approvals for any product candidates we develop independently;
- the cost of commercialization activities, if any, of any product candidates we develop independently that are approved for sale, including marketing, sales and distribution costs;
- the timing and amount of any sales of our product candidates, if any, or royalties thereon;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patents, including any litigation costs and the outcomes of any such litigation; and
- potential fluctuations in foreign currency exchange rates.

Accordingly, if we do not generate sufficient funding from our existing collaboration and any future collaborations, we will need to obtain additional funding to support our operations. Additional funds may not be available if and when we need them, on terms that are acceptable to us, or at all. Our ability to raise funds will depend on financial, economic and market conditions and other factors, many of which are beyond our control. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate preclinical studies, clinical trials or other research and development activities for one or more of our product candidates.

***We have not developed independently any approved products and we have limited clinical development experience, which makes it difficult to assess our ability to develop and commercialize our product candidates.***

AbbVie has been responsible for all of the clinical development of our HCV protease inhibitor products. We have not yet demonstrated an ability to address successfully many of the risks and uncertainties associated with late-stage clinical development, regulatory approval and commercialization of therapeutic products such as the ones we plan to develop independently. For example, to execute our business plan for the development of our independent RSV and HBV programs, we will need to successfully:

- execute clinical development of our product candidates and demonstrate acceptable safety and efficacy for them alone or in combination with other drugs or drug candidates;
- obtain required regulatory approvals for the development and commercialization of our product candidates;
- develop and maintain any future collaborations we may enter into for any of these programs;
- obtain and maintain patent protection for our product candidates and freedom from infringement of intellectual property of others;
- establish acceptable commercial manufacturing arrangements with third-party manufacturers;
- build and maintain robust sales, distribution and marketing capabilities, either independently or in collaboration with future collaborators;

- gain market acceptance for our product candidates among physicians, payors and patients; and
- manage our spending as costs and expenses increase due to clinical trials, regulatory approvals and commercialization.

If we are unsuccessful in accomplishing these objectives, we may not be able to successfully develop and commercialize our product candidates and expand our business or continue our operations.

***If we are not successful in developing EDP-938, EDP-235, EDP-514 and/or EDP-323, or in discovering further product candidates, our ability to expand our business and achieve our strategic objectives will be impaired.***

Much of our internal research is at preclinical stages. Research programs designed to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying additional potential product candidates, yet fail to yield product candidates for clinical development or commercialization for many reasons, including the following:

- the research methodology used may not be successful in identifying additional potential product candidates;
- competitors may develop alternatives that render our product candidates less commercially viable or obsolete;
- competitors may obtain intellectual property protection that effectively prevents us from developing a product candidate;
- a product candidate may, on further study, be shown not to be an effective treatment in humans or to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria; and
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all.

Additional drug candidates that we may develop will require significant research, preclinical and clinical studies, regulatory approvals and commitments of resources before they can be commercialized. We cannot give assurance that our research will lead to the discovery of any additional drug candidates that will generate additional revenue for us. If we are unable to identify additional compounds suitable for preclinical and clinical development, we may not be able to obtain sufficient product revenue in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

***The COVID-19 pandemic has had an impact on our business operations and clinical trials and could continue, directly or indirectly, to adversely affect our business, results of operations and financial condition and our stock price.***

The COVID-19 pandemic has had an impact on our business operations and we continue to monitor applicable government recommendations. We had to make modifications to our normal operations because of the COVID-19 pandemic, including allowing certain of our employees to work remotely and conducting our laboratory operations at reduced capacity. Now that almost all of our employees are vaccinated and levels of COVID-19 infection in Eastern Massachusetts have declined substantially, we have our laboratory operations back at full capacity and other operations have returned to more on-site activity. Notwithstanding these recent trends, the emergence of any new, more virulent SARS-CoV-2 variant that evades immunity from vaccination or prior infection could affect the health and availability of our workforce as well as those of the third parties whom we are relying on to take similar measures. As a result, we may experience new disruptions to our business operations and our business could be materially adversely affected further, directly or indirectly, by COVID-19. Organizations and individuals may continue to take steps to avoid or reduce infection, including limiting travel and staying home from work.

The extent and severity of the impact on our business and clinical trials will be determined largely by the extent of disruptions in the supply chains for our research and clinical trial materials, delays in the conduct and recruitment of current and future clinical trials and reductions in the number of patients accessing AbbVie's HCV regimens. For example, we paused recruitment for two of our studies in March 2020, but we were able to resume recruitment of these studies in July 2020. In addition, the public health response to the COVID-19 pandemic, including lock-downs, mask mandates, social distancing and other mitigation steps to manage the COVID-19 pandemic significantly reduced the incidence of RSV and other respiratory illnesses worldwide. We have made extensive efforts to expand our RSV clinical trial sites beyond North America, including sites across Europe, the Asia-Pacific and the Southern Hemisphere, to be ready when RSV infection fully re-emerges globally, but we cannot predict when that may occur. These impacts of COVID-19 could continue to affect the future course of our RSV studies and delay their timelines.

COVID-19 has also impacted new HCV patient starts in both the United States and the rest of the world, resulting in a decline in sales of HCV treatments compared with pre-COVID-19 levels. While new HCV infections are continuing, at this time it is uncertain when and the extent to which treatment of new HCV patients and revenues will return to pre-COVID-19 levels.

Although it is not possible at this time to estimate the entirety of the impact that the COVID-19 pandemic will have on our business, operations and employees, our contract manufacturers, our preclinical and clinical research contractors, and our collaborators in

clinical research, any continued spread of COVID-19, measures taken by governments, actions taken to protect employees from this disease, and the broad impact of the pandemic on all business activities, may materially and adversely affect our business, results of operations and financial condition and our stock price. Additionally, if new, more infectious and virulent variants emerge, it is possible that the impact of the pandemic on our business may increase or lengthen in duration.

***If we fail to attract and keep senior management and key scientific personnel, we may be unable to successfully develop our product candidates, conduct our clinical trials and commercialize our product candidates.***

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. We are highly dependent upon our senior management, particularly Jay R. Luly, Ph.D., our Chief Executive Officer and President, Yat Sun Or, Ph.D., our Senior Vice President, Research and Development and Chief Scientific Officer, and Scott T. Rottinghaus, M.D., our Senior Vice President and Chief Medical Officer whom we hired in August 2022, as well as other employees and consultants. Although none of Drs. Luly, Or, or Rottinghaus has informed us to date that he expects to retire or resign in the near future, the loss of the services of any of these individuals or one or more of our other members of senior management could delay or prevent the successful development of our product candidates.

While we have not historically experienced unique difficulties attracting and retaining qualified employees, we could experience such problems in the future. For example, competition for qualified personnel in the biotechnology and pharmaceutical fields is intense. In addition, we will need to hire additional personnel as we expand our clinical development and ultimately seek regulatory approvals and prepare for commercial activities. We may not be able to attract and retain quality personnel on acceptable terms.

***We may encounter difficulties in managing our growth and expanding our operations successfully.***

As we expand our research efforts and seek to advance our product candidates through clinical trials, we will need to expand our development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to obtain these capabilities. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and clinical trials effectively and hire, train and integrate additional management, administrative and sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our company.

## **Risks Related to Development, Clinical Testing and Regulatory Approval of Our Product Candidates**

***Clinical drug development involves a lengthy and expensive process with uncertain timelines and uncertain outcomes. Any ongoing or future clinical trials of our product candidates may fail to demonstrate sufficient safety and efficacy. If clinical trials of any of our proprietary product candidates are prolonged or delayed or fail, we may be unable to commercialize our product candidates on a timely basis or ever.***

Clinical testing is expensive and, depending on the stage of development, can take a substantial time period to complete. Its outcome is inherently uncertain, and failure can occur at any time during clinical development. None of our product candidates in our pipeline other than glecaprevir, which was clinically developed by AbbVie, has yet to advance beyond Phase 2 clinical trials. Any ongoing or future clinical trials of our product candidates may fail to demonstrate sufficient safety and efficacy. Moreover, regulatory and administrative delays, including those caused by the COVID-19 pandemic, for any product candidate in our pipeline may adversely affect our or any future collaborator's clinical development plans and jeopardize our or any future collaborator's ability to attain product approval, commence product sales and compete successfully against other therapies.

Clinical trials can be delayed for a variety of reasons, including delays related to:

- reaching an agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- failure of third-party contractors, such as CROs, or investigators to comply with regulatory requirements;
- failure to obtain on a timely basis, or at all, the necessary approvals from regulators or institutional review boards, or IRBs, to commence a clinical trial at a prospective trial site, or their suspension or termination of a clinical trial once commenced;
- difficulty in recruiting suitable patients to participate in a trial;

- the impact of the COVID-19 pandemic on the ability of CROs to conduct their own operations, resulting in, among other things, delays in recruitment or dosing of our clinical trials;
- the broader impact of the COVID-19 pandemic on the incidence of other viruses (e.g., RSV and hMPV), the economic challenges for clinical trial sites and the political and socio-economic stability affecting their operations generally;
- seasonality and variations in the incidence of infection year to year (e.g. RSV) affecting enrollment in clinical trials;
- difficulty in having patients complete a trial or return for post-treatment follow-up;
- clinical sites deviating from trial protocol or dropping out of a trial;
- problems with drug product or drug substance storage and distribution;
- having to add new clinical trial sites;
- our inability to manufacture, or obtain from third parties, adequate supply of drug product sufficient to complete our preclinical studies and clinical trials;
- changes in governmental or regulatory administration;
- lack of clear guidance or changes in regulatory requirements, policy and guidelines, including guidelines specifically addressing requirements for the development of treatments for RSV, COVID-19, HBV or hMPV infection;
- difficulty in obtaining and maintaining adequate insurance coverage;
- program discontinuations or clinical holds for a program of a competitor, which could increase the level of regulatory scrutiny or delay data review or other response times by regulators with respect to one of our programs in the same class as the competitor's program; or
- varying interpretations of data by the FDA, the EMA and similar foreign regulatory agencies.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trial is being conducted, by any Data Safety Monitoring Board, or DSMB, for such trial, or by the FDA, the EMA or other regulatory authorities. Such authorities may impose such a suspension or termination 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 drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, delays can occur due to safety concerns arising from trials or other clinical data regarding another company's product candidate in the same compound class as one of ours. If we or any future collaborators experience delays in the completion of, or termination of, any clinical trial of one of our product candidates, the commercial prospects of the product candidate will be harmed, and our ability to commence product sales and generate product revenues from the product candidate will be delayed. In addition, any delays in completing our clinical trials will increase our costs in the long term and slow down our product candidate development and approval process. Any of these occurrences may harm our business, financial condition and prospects significantly. 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.

***We may choose to test any of our clinical candidates preclinically and/or clinically in combination with other compounds with different mechanisms of action, and any adverse results from such testing may have adverse consequences for the further development potential of not only the combination but also the clinical candidate itself as a monotherapy or in combination with other mechanisms of action.***

We expect that the further development of successful therapies in our principal disease area of HBV may require combining one or more of our compounds with other compounds with different mechanisms of action. To advance our programs and achieve favorable opportunities for any such combinations we may conduct preclinical testing, as well as clinical testing, with one of our other compounds or with a compound of a third party, with or without a longer-term collaboration with any such party. We may choose to disclose such testing in advance, but we can anticipate that some of the testing would be done without any public disclosure. If any such testing produces adverse results, we may have to disclose it to regulatory authorities as part of the data available with respect to our product candidate and the data may have adverse consequences for the further development and the ultimate conditions attached to any approved use of the product candidate, whether in the combination tested or even as a monotherapy or in combination with other mechanisms.



***EDP-938, EDP-235, EDP-514, or EDP-323, or any other product candidate emerging from our current research programs may have undesirable side effects which may delay or prevent marketing approval, or, if approval is received, require our product candidate to be taken off the market, require us to include safety warnings or otherwise limit sales.***

In our RSV program, we are developing inhibitors of the N-protein and L-protein. No inhibitor of the RSV N- or L-protein has progressed beyond a Phase 2 clinical trial, so we are not yet able to assess the potential liabilities of an N-protein or L-protein inhibitor in large scale studies or in the general population. In addition, the principal target populations in RSV, namely infants, the elderly, and the immunocompromised, represent sensitive patient populations that could be more prone to adverse effects of therapy.

In our SARS-CoV-2 program, we have designed EDP-235 as a 3CL protease inhibitor specifically for the SARS-CoV-2 virus. We recently started testing EDP-235 in humans and, therefore, any long-term or rare potential side effects are unknown. While scientific understanding of the longer-term effects of COVID-19, also known as long-COVID, are still emerging and being studied, it may be difficult to determine whether any unexpected downstream effects after treatment with EDP-235 are due to that drug or the infection itself.

In our HBV program, we have developed modulators of capsid assembly, also known as core inhibitors. No capsid assembly modulators have advanced beyond Phase 2 clinical studies, and thus we are not able to predict what adverse effects may arise in longer studies conducted in larger populations. In addition, no mechanisms or combination of mechanisms with a finite treatment duration have resulted in a sustained viral response, so it is unknown what role a core inhibitor mechanism may play in HBV therapy.

If any of our product candidates receives marketing approval and we or others later identify undesirable or unacceptable side effects caused by such products:

- regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies;
- we may be required to change instructions regarding the way the product is administered, conduct additional clinical trials or change the labeling of the product;
- we may be subject to limitations on how we may promote the product;
- the product may be subject to additional distribution restrictions under a REMS, if required by the FDA;
- sales of the product may decrease significantly;
- regulatory authorities may require us to take our approved product off the market;
- we may be subject to litigation or product liability claims; and
- our reputation and our stock price may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product or could substantially increase commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenue from the sale of any product we develop.

***If we are required to suspend or discontinue clinical trials due to side effects or other safety risks associated with our product candidates, or if we are required to conduct studies on the long-term effects associated with the use of any of those product candidates, then commercialization any of those product candidates could be delayed or halted.***

Clinical trials involving our product candidates may be suspended or terminated at any time for a number of safety-related reasons. For example, we may voluntarily suspend or terminate clinical trials if at any time one of our product candidates, or a combination therapy including any of them, presents an unacceptable safety risk to the clinical trial patients. In addition, IRBs or regulatory agencies may order the temporary discontinuation or termination of clinical trials at any time if they believe that the clinical trials are not being conducted in accordance with applicable regulatory requirements, including if they present an unacceptable safety risk to patients. Administering any product candidate to humans may produce undesirable side effects. The existence of undesirable side effects resulting from any of our product candidates, or a combination therapy including any of them, could cause us or regulatory authorities, such as the FDA or EMA, to interrupt, delay or halt clinical trials of our product candidates and could result in the FDA or EMA or other regulatory agencies denying further development or approval of our product candidates for any or all targeted indications. This, in turn, could prevent us from commercializing our product candidates.

***Results of earlier clinical trials may not be predictive of the results of later-stage clinical trials.***

To date we have only tested our product candidates through initial Phase 2 studies. The results of preclinical studies and these early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials, if any. In addition, results of

Phase 3 clinical trials in one or more ethnic groups are not necessarily indicative of results in other ethnic groups. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy results despite having progressed through preclinical studies and initial clinical trials. For example, several companies engaged in clinical development in the disease areas we are also engaged in have suffered significant setbacks in advanced clinical trials due to adverse safety profiles or lack of efficacy, notwithstanding promising results in earlier studies. Similarly, future clinical trial results may not be successful for these or other reasons.

Product candidate development risk is heightened by any changes in the planned clinical trials compared to the completed clinical trials. As product candidates are developed through preclinical studies and early-stage and late-stage clinical trials towards approval and commercialization, it is customary that various aspects of the development program, such as manufacturing and formulation, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could make the results of planned clinical trials or other future clinical trials we may initiate less predictable and could cause our product candidates to perform differently, which could delay completion of clinical trials, delay approval of our product candidates and/or jeopardize our ability to commence product sales and generate revenues.

***The regulatory approval processes of the FDA, the EMA and other comparable foreign authorities are lengthy, time-consuming and inherently unpredictable, and if we are ultimately unable to obtain timely regulatory approval for our product candidates, our business will be substantially harmed.***

The regulatory approval process is expensive and, while the time required to gain FDA and foreign regulatory approval is uncertain, it may take years. Regulatory approvals are unpredictable and depend upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of preclinical and clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We may be required to undertake and complete certain additional preclinical studies to generate toxicity and other data required to support the submission of a New Drug Application, or NDA, to the FDA or comparable application to other regulatory authorities. AbbVie obtained all regulatory approvals for its paritaprevir-containing regimens and for MAVYRET/MAVIRET, which contains glecaprevir. We have not obtained regulatory approval by ourselves for any of our wholly-owned product candidates and it is possible that none of our existing product candidates or any of our future product candidates will ever obtain regulatory approval. Furthermore, approval in the United States by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA, the EMA or other comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA, the EMA or other comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA, the EMA or other comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA, the EMA or other comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA or other submissions or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies of any of our product candidates; and
- the approval policies or regulations of the FDA, the EMA or other comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

We cannot be assured that after spending substantial time and resources, we will obtain regulatory approvals in any desired jurisdiction. Even if we were to obtain approval, regulatory authorities 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. Significant clinical trial delays could allow our competitors to obtain marketing approval before we do or could in effect shorten the patent protection period during which we may have the exclusive right to commercialize our product candidates. In addition, it may ultimately not be possible to achieve the prices intended for our products. In many foreign countries, including those in the European Union, a product candidate must be approved for

reimbursement before it can be approved for sale in that country. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates and our business.

***The regulatory pathway for approval of a therapeutic treatment for COVID-19 such as EDP-235 is continually evolving and may result in unexpected or unforeseen challenges and longer timelines than seen for earlier COVID-19 vaccines and therapeutics.***

The FDA has the authority to grant an emergency use authorization, or EUA, to allow unapproved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions when there are no adequate, approved, and available alternatives. To date, COVID-19 vaccines, therapeutic antibodies and other therapeutics that have demonstrated positive results in clinical trials have moved rapidly through the FDA regulatory review and EUA process, as well as the review and authorization process in a number of other jurisdictions, including the EU. The speed at which all parties are acting to create and test many therapeutics for COVID-19 is unusual, while evolving or changing plans or priorities within the FDA or the regulatory authorities in other jurisdictions, including changes based on new data regarding potential therapeutics of others, and new variants of the virus, may significantly affect the regulatory timeline for further authorizations or approvals for therapeutics such as EDP-235. Moreover, there is not yet any clear definition of the point at which the FDA will determine that the underlying COVID-19 health emergency no longer exists or warrants such authorizations. Accordingly, if there are successful clinical trials of EDP-235 demonstrating its therapeutic benefit and safety profile, it is still uncertain what will be the timelines or regulatory processes required for the authorization or approval of EDP-235 as a treatment for COVID-19.

***Even if we receive regulatory approval for any of our product candidates we develop independently, we will be subject to ongoing FDA obligations and continued regulatory review in other jurisdictions, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we or our collaborators fail to comply with regulatory requirements or experience unanticipated problems with our products.***

Any regulatory approvals that we receive for our product candidates we develop independently may be subject to limitations on the approved indicated uses for which the product may be marketed or subject to certain conditions of approval, or may contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product candidate.

In addition, if the FDA approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, as well as continued compliance with current good manufacturing practices, or cGMP, and good clinical practices, or GCP, for any clinical trials that we or our collaborators conduct post-approval. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

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

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we, or AbbVie in the case of any licensed HCV product, are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or AbbVie are not able to maintain regulatory compliance, our product candidates or AbbVie's licensed HCV products may lose any marketing approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

***We may delay 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, which could materially harm our business and adversely affect our stock price.***

Even though 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. Such a delay, suspension or termination could materially harm our business, results of operations or financial condition.

## **Risks Related to Commercialization of Our Product Candidates**

***Unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives in the United States could harm our business.***

The regulations that govern marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. In the United States, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, collectively referred to as the ACA, has significantly changed the way healthcare is financed by both governmental and private insurers. While we cannot predict what impact on federal reimbursement policies this law or any amendment to it will continue to have in general or specifically on MAVYRET/MAVIRET or any product or regimen that we may commercialize, the ACA or any such amendment may result in downward pressure on pharmaceutical reimbursement, which could negatively affect market acceptance of new products. In addition, several states have not implemented the provisions of the ACA that involve the expansion of Medicaid-eligibility for low-income adults. While the United States Supreme Court recently rejected the latest challenge to the constitutionality of the ACA, it is possible that other legislative efforts may seek to modify it. We cannot predict what effect any legislation may have on us or on AbbVie's sales of MAVYRET/MAVIRET. In addition, other legislative changes have been proposed since the Affordable Care Act was enacted. There has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Most recently, the Inflation Reduction Act of 2022, or IRA, which, among other provisions, included several measures intended to lower the cost of prescription drugs and related healthcare reforms. Specifically, the Act authorizes and directs the Department of Health and Human Services, or DHHS, to set drug price caps for certain high-cost Medicare Part B and Part D qualified drugs, with the initial list of drugs to be selected by September 1, 2023, and the first year of maximum price applicability to begin in calendar year 2026. The Act further authorizes the DHHS to penalize pharmaceutical manufacturers that increase the price of certain Medicare Part B and Part D drugs faster than the rate of inflation. Finally, the Act creates significant changes to the Medicare Part D benefit design by capping Part D beneficiaries' annual out-of-pocket spending beginning in calendar year 2025. We cannot be sure whether additional or related legislation or rulemaking will be issued or enacted, or what impact, if any, such changes will have on the royalty revenue we receive from MAVYRET/MAVIRET or revenue from any of our drug candidates, if approved for commercial use, in the future. If any further healthcare reform measures adopted in the future result in additional downward pressure on the price that AbbVie receives for MAVYRET/MAVIRET, this would adversely affect our future revenues, and the price of our common stock could be materially adversely affected.

Our ability to commercialize any product candidate successfully, as well as AbbVie's continued commercialization of MAVYRET/MAVIRET, will also depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. In the case of HCV, limitations of coverage have recently been used to limit access to HCV treatments for only those patients with more advanced fibrosis. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and, in many cases involving HCV drugs, seeking discounts in exchange for greater patient access to a particular HCV drug. In addition, there are private and public payors challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product that we may commercialize and, if reimbursement is available, the level of reimbursement. In addition, reimbursement may impact the demand for, or the price of, MAVYRET/MAVIRET or any product candidate for which we may obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we may seek marketing approval.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or comparable authorities in other jurisdictions. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also be insufficient to cover our and any collaborator's costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. AbbVie's inability to continue to obtain coverage and profitable payment rates from both government-funded and private payors for MAVYRET/MAVIRET, or our inability



to obtain the same for any product candidate that we develop, could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

In general, the United States and several other jurisdictions are considering a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. We expect to experience pricing pressures in connection with the sale of any products that we develop or that are being commercialized under our collaboration with AbbVie. The implementation of cost containment measures or other healthcare reforms may limit our ability to generate revenue, maintain profitability or commercialize our product candidates.

***There is significant uncertainty around the future path of the COVID-19 pandemic, which may impact opportunity of EDP-235 as a potential treatment for COVID-19.***

COVID-19 is currently still an ongoing global pandemic and there is an urgent need for a safe and effective oral treatment for it. However, the longevity and extent of the COVID-19 pandemic are unpredictable, and it is uncertain whether SARS-CoV-2 will become an endemic seasonal respiratory disease, such as RSV or flu, after the current pandemic has subsided. If the pandemic were to end with a substantial decrease in new infections, due to the effectiveness of vaccines or otherwise, there would be a reduced opportunity for EDP-235.

In order to prepare for the possibility that EDP-235 is successful in development and commercialization, we are currently devoting resources towards executing on an accelerated development path, including sufficient drug supply for advanced clinical trials and commercialization. If EDP-235 does not advance in development or is not approved for the treatment of COVID-19, or if infection rates decrease substantially, we may not be able to recover these costs and our results of operations and financial condition would be adversely affected.

***Foreign governments tend to impose strict price controls, which may adversely affect our future profitability.***

In most foreign countries, particularly in the European Union and Japan, prescription drug pricing and/or reimbursement is subject to governmental control. In those countries that impose price controls, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies.

Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we (or AbbVie in the case of MAVYRET/MAVIRET) might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay the commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues that are generated from the sale of the product in that country. If reimbursement of MAVYRET/MAVIRET or of any of our product candidates is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, or if there is competition from lower priced cross-border sales, our results of operations will be negatively affected.

***If, in the future, we are unable to establish our own sales, marketing and distribution capabilities or enter into licensing or collaboration agreements for these purposes, we may not be successful in commercializing any product candidates.***

We do not have a sales or marketing infrastructure and have no sales, marketing or distribution experience. We will seek to either build our own commercial infrastructure to commercialize any products if and when they are approved, or enter into licensing or collaboration agreements where our collaborator is responsible for commercialization, as in the case of our collaboration with AbbVie, or where we have the right to assist in the future development and commercialization of such products.

To develop internal sales, distribution and marketing capabilities, we will have to invest significant amounts of financial and management resources, some of which will be committed prior to any confirmation that any of our proprietary product candidates will be approved. For product candidates for which we decide to perform sales, marketing and distribution functions ourselves, we could face a number of additional risks, including:

- 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 any 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; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

Where and when appropriate, we may elect to utilize contract sales forces or distribution partners to assist in the commercialization of our product candidates. If we enter into arrangements with third parties to perform sales, marketing and distribution services for our products, the resulting revenues or the profitability from these revenues to us are likely to be lower than if we had sold, marketed and distributed our products ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of these third parties may fail to devote the necessary resources and attention to sell, market and distribute our products effectively.

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

***Commercial success of our product candidates depends upon significant market acceptance among physicians, patients and healthcare payors of any resulting approved drug.***

EDP-938, EDP-235, EDP-514, and EDP-323 and any other product candidate that we may develop in the future, whether as part of a combination therapy or as a monotherapy, are subject to market acceptance among physicians, healthcare payors, patients and the medical community. The degree of market acceptance of any product candidate for which we obtain approval for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of treatment regimens containing one of our product candidates, as demonstrated in clinical trials, and the degree to which these regimens represent a clinically meaningful improvement in care as compared with other available therapies;
- the clinical indications for which any treatment regimen containing one of our product candidates become approved;
- acceptance among physicians, major operators of clinics, payors and patients of any treatment regimen containing one of our product candidates;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the potential and perceived advantages of treatment regimens containing one of our product candidates over alternative treatments;
- the cost of treatment of regimens containing one of our product candidates in relation to the cost of alternative treatments;
- the availability of adequate reimbursement and pricing by third parties and government authorities and successful negotiation of favorable agreements with payors by us or any collaborator of ours, as well as the impact of any agreements among any of the foregoing and one or more of our competitors limiting access to our product in favor of one or more competitive products;
- the continued longevity of any market for which we develop a drug;
- the levels of funding provided by government-funded healthcare for treatment of any disease for which we develop a drug;
- the relative convenience and ease of administration of any treatment regimen containing one of our product candidates compared to competitive regimens;
- the prevalence and severity of adverse side effects, whether involving the use of treatment regimens containing one of our products candidates or similar, competitive treatment regimens; and
- the effectiveness of our sales and marketing efforts.

If treatment regimens containing one of our product candidates are approved and then fail to achieve market acceptance, we may not be able to generate significant additional revenue. Further, if new, more favorably received therapies are introduced after any such regimen achieves market acceptance, then we may not be able to maintain that market acceptance over time.

## Risks Related to Our Dependence on Third Parties

***We may not be successful in establishing new product collaborations, which could adversely affect our ability to develop and commercialize one or more of our product candidates. If we are unsuccessful in maintaining or forming alliances on favorable terms, our business may not succeed.***

We may seek to enter into additional product collaborations in the future, including alliances with other biotechnology or pharmaceutical companies, to enhance and accelerate the development and commercialization of one or more of our product candidates. For example, we plan to out-license our FXR agonist candidates for combination therapy for NASH and are seeking potential partners for this program. We face significant competition in seeking appropriate collaborators and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish other product collaborations or other alternative arrangements for any product candidates and programs because our research and development pipeline may be insufficient, our product candidates and programs may be deemed to be at too early of a stage of development for collaborative effort and/or third parties may not view our product candidates and programs as having the requisite potential to demonstrate safety and efficacy. Even if we are successful in our efforts to establish product collaborations, the terms that we agree upon may not be favorable to us and we may not be able to maintain such product collaborations if, for example, development or approval of a product candidate is delayed or sales of an approved product are disappointing.

If our existing collaboration agreement with AbbVie is terminated, or if we determine that entering into other product collaborations is in our best interest but we either fail to enter into, experience a delay in entering into, or fail to maintain, such collaborations:

- the development of certain of our product candidates may be terminated or delayed;
- our cash expenditures related to the development of certain of our product candidates would increase significantly and we may need to seek additional financing;
- we may be required to hire additional employees or otherwise develop expertise, such as clinical, regulatory, sales and marketing expertise, which we do not currently have;
- we will bear all of the risk related to the development of any such product candidates; and
- the competitiveness of any product candidate that is commercialized could be reduced.

***We intend to rely on third-party manufacturers to produce our development-stage product candidate supplies and any commercial supplies of any approved product candidates. Any failure by a third-party manufacturer to produce acceptable supplies for us may delay or impair our ability to initiate or complete our clinical trials or sell any resulting product.***

We do not currently own or operate any manufacturing facilities. We plan to continue to work with third-party contract manufacturers to produce sufficient quantities of any product candidates for preclinical testing, clinical trials and commercialization. If we are unable to arrange for such a third-party manufacturing source for any of our product candidates, or fail to do so on commercially reasonable terms, we may not be able to successfully produce, develop and market one or more of our product candidates, or we may be delayed in doing so.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured product candidates ourselves, including reliance on the third party for regulatory compliance and quality control and assurance, volume production, the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control (including a failure to synthesize and manufacture our product candidates in accordance with our product specifications), shutdowns of manufacturing sites or other supply chain constraints resulting from the COVID-19 pandemic, and the possibility of termination or nonrenewal of the agreement by the third party at a time that is costly or damaging to us. In addition, the FDA and other regulatory authorities require that our product candidates be manufactured according to cGMP and similar foreign standards. Pharmaceutical manufacturers and their subcontractors are required to register their facilities and/or products manufactured at the time of submission of the marketing application and then annually thereafter with the FDA and certain state and foreign agencies. They are also subject to periodic unannounced inspections by the FDA, state and other foreign authorities. Any subsequent discovery of problems with a product, or a manufacturing or laboratory facility used by us or our collaborators, may result in restrictions on the product or on the manufacturing or laboratory facility, including marketed product recall, suspension of manufacturing, product seizure, or a voluntary withdrawal of the drug from the market. Any failure by our third-party manufacturers to comply with cGMP or failure to scale up manufacturing processes, including any failure to deliver sufficient quantities of product candidates in a timely manner, could lead to a delay in, or failure to obtain, regulatory approval of any of our product candidates.

We plan to rely on third-party manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical studies. There are a small number of suppliers for certain capital equipment and materials that we plan to use to manufacture our drugs. Such suppliers may not sell these materials to our manufacturers at the times we need them or on

commercially reasonable terms. Moreover, we currently do not have any agreements for the production of these materials. Although we do not intend to begin a clinical trial unless we believe we have a sufficient supply of a product candidate to complete the clinical trial, any significant delay in the supply of a product candidate or the material components thereof for an ongoing clinical trial due to the need to replace a third-party manufacturer could considerably delay completion of our clinical studies, product testing and potential regulatory approval of our product candidates. If our manufacturers or we are unable to purchase these materials after regulatory approval has been obtained for our product candidates, the commercial launch of our product candidates would be delayed or there would be a shortage in supply, which would impair our ability to generate revenue from the sale of our product candidates.

Contract manufacturers may not be able to manufacture our product candidates at a cost or in quantities or in a timely manner necessary to develop and commercialize them. If we successfully commercialize any of our product candidates, to meet our projected needs we may need to find third parties that will increase their scale of production, or we may have to establish or access large-scale commercial manufacturing capabilities. We may require additional funds, personnel and other resources to build, lease or operate any manufacturing facility.

***A portion of our research and a portion of our manufacturing of certain key intermediates used in the manufacture of the active pharmaceutical ingredients for our product candidates takes place in China through third-party researchers and manufacturers. A significant disruption in the operation of those researchers or manufacturers, or a trade war, political unrest or an epidemic in China, such as the COVID-19 pandemic, could materially adversely affect our business, financial condition and results of operations.***

Although manufacturing for MAVYRET/MAVIRET is being conducted by AbbVie, we have relied on third parties located in China to manufacture and supply certain key intermediates used in the manufacture of our active pharmaceutical ingredients, or API, for our current product candidates, and we expect to continue to use such third party manufacturers for such intermediates for any product candidates we develop independently. Any disruption in production or inability of our manufacturers in China to produce adequate quantities to meet our needs, whether as a result of a natural disaster, pandemics 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. We also use contract researchers in China to conduct a portion of our research for our early-stage programs. Any disruption in the team conducting that research could cause delays in one or more of our research programs and could require us to curtail one or more programs, at least until we could contract for that research to be done elsewhere. For example, either of these risks could be triggered by an epidemic such as the outbreak of COVID-19 in the Wuhan region of China or the continuing series of so-called “lock-downs” in China when strict quarantine requirements are imposed on large population areas in response to new incidents of COVID infection. To date, our contract manufacturers in China, which are not located in the Wuhan region, have avoided any material delays in their ability to deliver API and other services through extraordinary efforts, including temporarily housing staff in the manufacturing facility. Furthermore, since these researchers and manufacturers are located in China, we are exposed to the possibility of product supply disruption and increased costs in the event of changes in the policies of the United States or Chinese governments, political unrest or unstable economic conditions in China. For example, a trade war could lead to tariffs on the chemical intermediates we use that are manufactured in China. Any of these matters could materially and adversely affect our business and results of operations. Any recall of the manufacturing lots or similar action regarding our API used in clinical trials could delay the trials or detract from the integrity of the trial data and its potential use in future regulatory filings. In addition, manufacturing interruptions or failure to comply with regulatory requirements by any of these manufacturers could significantly delay clinical development of potential products and reduce third-party or clinical researcher interest and support of proposed trials. These interruptions or failures could also impede commercialization of our product candidates and impair our competitive position. Further, we may be exposed to fluctuations in the value of the local currency in China. Future appreciation of the local currency could increase our costs. In addition, our labor costs could continue to rise as wage rates increase due to increased demand for skilled laborers and the availability of skilled labor declines in China.

***We will rely on third parties to monitor, support, conduct and/or oversee clinical trials of our product candidates that we develop independently and, in some cases, to maintain regulatory files for those product candidates. If we are not able to maintain or secure agreements with such third parties on acceptable terms, if these third parties do not perform their services as required, or if these third parties fail to timely transfer any regulatory information held by them to us, we may not be able to obtain regulatory approval for, or commercialize, our product candidates.***

We will rely on CROs, hospitals, clinics, academic institutions and other third-party collaborators who are outside our control to monitor, support, conduct and/or oversee preclinical and clinical studies of our product candidates. We will also rely on third parties to perform clinical trials of our product candidates when they reach that stage. As a result, we have less control over the timing and cost of these studies and the ability to recruit trial subjects than if we conducted these trials wholly by ourselves. If we are unable to maintain or enter into agreements with these third parties on acceptable terms or engagement is terminated, we may be unable to enroll patients on a timely basis or otherwise conduct our trials in the manner we anticipate. In the case of our ongoing studies, we paused recruitment and dosing as a result of the COVID-19 pandemic in March 2020, but we were able to resume the studies in July 2020.



The pause in these studies delayed their completion, and it is uncertain whether any of our other ongoing studies may be subject to further disruptions due to the pandemic. In addition, there is no guarantee that these third parties will devote adequate time and resources to our studies or perform as required by a contract or in accordance with regulatory requirements, including maintenance of clinical trial information regarding our product candidates. If these third parties fail to meet expected deadlines, fail to timely transfer to us any regulatory information, fail to adhere to protocols or fail to act in accordance with regulatory requirements or our agreements with them, or if they otherwise perform in a substandard manner or in a way that compromises the quality or accuracy of their activities or the data they obtain, then clinical trials of our product candidates may be extended, delayed or terminated, or our data may be rejected by the FDA or regulatory agencies.

***To the extent we elect to enter into additional licensing or collaboration agreements to partner our product candidates, our dependence on such relationships may adversely affect our business.***

Our commercialization strategy for some of our product candidates may depend on our ability to enter into collaboration agreements with other companies to obtain access to other compounds for use in combination with any of our product candidates or for assistance and funding for the development and potential commercialization of any of these product candidates, similar to what we have done with AbbVie. Supporting diligence activities conducted by potential collaborators and negotiating the financial and other terms of a collaboration agreement are long and complex processes with uncertain results. Even if we are successful in entering into one or more additional collaboration agreements, collaborations can involve greater uncertainty for us, as we may have limited or no control over certain aspects of our collaborative programs. We may determine that continuing a collaboration under the terms provided is not in our best interest, and we may terminate the collaboration. Our collaborators could delay or terminate their agreements with us, and our product candidates subject to collaborative arrangements may never be successfully commercialized.

Further, our collaborators may develop alternative products or pursue alternative technologies either on their own or in collaboration with others, including our competitors, and the priorities or focus of our collaborators may shift such that our programs receive less attention or resources than we would like, or they may be terminated altogether. Any such actions by our collaborators may adversely affect our business prospects and ability to earn revenue. In addition, we could have disputes with our collaborators, such as the interpretation of terms in our agreements. Any such disagreements could lead to delays in the development or commercialization of any potential products or could result in time-consuming and expensive litigation or arbitration, which may not be resolved in our favor.

Even with respect to programs that we intend to commercialize ourselves, we may enter into agreements with collaborators to share in the burden of conducting clinical trials, manufacturing and marketing our product candidates or products. In addition, our ability to apply our proprietary technologies to develop proprietary compounds will depend on our ability to establish and maintain licensing arrangements or other collaborative arrangements with the holders of proprietary rights to such compounds. We may not be able to establish such arrangements on favorable terms or at all, and our collaborative arrangements may not be successful.

## **Risks Related to Our Intellectual Property Rights**

***We are competing to develop intellectual property in areas of small-molecule drug development that are highly competitive. We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our product candidates.***

Our commercial success will depend, in large part, on our ability to obtain and maintain patent and other intellectual property protection with respect to our product candidates. We cannot be certain that patents will be issued or granted with respect to our patent applications that are currently pending, or that issued or granted patents will not later be found to be invalid and/or unenforceable, be interpreted in a manner that does not adequately protect our products, or otherwise provide us with any competitive advantage. The patent position of biotechnology and pharmaceutical companies is generally uncertain because it involves complex legal and factual considerations. The standards applied by the United States Patent and Trademark Office and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and pharmaceutical patents. Consequently, patents may not issue from our pending patent applications. As such, we do not know the degree of future protection that we will have on our proprietary products and technology, if any, and a failure to obtain adequate intellectual property protection with respect to our product candidates and proprietary technology could have a material adverse impact on our business.

In addition, certain of our activities in the past have been funded, and others may in the future be funded, by the United States federal government. For example, the preclinical and early clinical development of the lead antibiotic product candidate in our former antibiotic program, which we are no longer developing, was funded under a contract with NIAID, an entity of the United States federal government. When new technologies are developed with United States federal government funding, the government obtains certain rights in any resulting patents, including a nonexclusive license authorizing the government to use the invention for non-commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise “march-in” rights to use or allow third parties to use our patented technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the United States government-funded

technology, or because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations or to give preference to United States industry. In addition, United States government-funded inventions must be reported to the government and United States government funding must be disclosed in any resulting patent applications. In addition, our rights in such inventions are subject to certain requirements to manufacture products in the United States.

***Claims that our product candidates or the sale or use of our products infringe the patent or other intellectual property rights of third parties could result in costly litigation or could require substantial time and money to resolve, even if litigation is avoided.***

Our commercial success depends upon our ability to develop, manufacture, market and sell our product candidates and use our proprietary technology without infringing the intellectual property rights of others. We cannot guarantee that our product candidates or any uses of our product candidates do not and will not in the future infringe third-party patents or other intellectual property rights. Third parties might allege that we or our collaborators are infringing their patent rights or that we have misappropriated their trade secrets, or that we are otherwise violating their intellectual property rights, whether with respect to the manner in which we have conducted our research or to the composition, use or manufacture of the compounds we have developed or are developing with our collaborators. Such third parties might resort to litigation against us or other parties we have agreed to indemnify, which litigation could be based on either existing intellectual property or intellectual property that arises in the future.

It is also possible that we failed to identify, or may in the future fail to identify, relevant patents or patent applications held by third parties that cover our product candidates. For example, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Other patent applications in the United States and several other jurisdictions are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Furthermore, publication of discoveries in the scientific or patent literature often lags behind actual discoveries. Therefore, we cannot be certain that we or our collaborators were the first to invent, or the first to file patent applications on, our product candidates or for their uses, or that our product candidates will not infringe patents that are currently issued or that are issued in the future. In the event that a third party has also filed a patent application covering one of our product candidates or a similar invention, we may have to participate in an adversarial proceeding, known as an interference, declared by the U.S. Patent and Trademark Office or its foreign counterpart to determine priority of invention. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our products or their use.

In order to avoid or settle potential claims with respect to any patent or other intellectual property rights of third parties, we may choose or be required to seek a license from a third party and be required to pay license fees or royalties or both, which could be substantial. These licenses may not be available on acceptable terms, or at all. Even if we were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced, by court order or otherwise, to cease some or all aspects of our business operations, if, as a result of actual or threatened patent or other intellectual property claims, we are unable to enter into licenses on acceptable terms. Further, we could be found liable for significant monetary damages as a result of claims of intellectual property infringement. For example, we have received, and may in the future receive, offers to license and demands to license from third parties claiming that we are infringing their intellectual property or owe license fees and, even if such claims are without merit, there can be no assurance that we will successfully avoid or settle such claims.

In addition, if AbbVie licenses or otherwise acquires rights to intellectual property controlled by a third party in various circumstances, for example, where a product could not be legally developed or commercialized in a country without the third-party intellectual property right, it is entitled under our collaboration agreement to decrease payments payable to us on a product-by-product basis and, in certain cases, on a country-by-country basis. Any of the foregoing events could harm our business significantly. Defending against claims of patent infringement, misappropriation of trade secrets or other violations of intellectual property rights could be costly and time consuming, regardless of the outcome. Thus, even if we were to ultimately prevail, or to settle at an early stage, such litigation could burden us with substantial unanticipated costs. In addition, litigation or threatened litigation could result in significant demands on the time and attention of our management team, distracting them from the pursuit of other company business. Claims that our product candidates or the sale or use of our future products infringe, misappropriate or otherwise violate third-party intellectual property rights could therefore have a material adverse impact on our business.

***Issued patents covering one or more of our product candidates could be found invalid or unenforceable if challenged in court.***

Despite measures we take to obtain patent and other intellectual property protection with respect to our product candidates and proprietary technology, any of our intellectual property rights could be challenged or invalidated. For example, if we were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable. The same could occur in our patent infringement suit recently brought against Pfizer regarding Paxlovid, its antiviral treatment for COVID-19, even though our '953 patent at issue does not cover EDP-235 or our other discovery efforts targeted at SARS-CoV-2. In patent litigation in the United States and in some other jurisdictions, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged

failure to meet any of several statutory requirements, for example, 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 United States Patent and Trademark Office, or the applicable foreign counterpart, or made a misleading statement, during prosecution. Although we believe that we have conducted our patent prosecution in accordance with the duty of candor and in good faith, the outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on a product candidate. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, other than in litigation like the Pfizer case, we would lose at least part, and perhaps all, of the patent protection on a product candidate. Even if a defendant does not prevail on a legal assertion of invalidity and/or unenforceability, our patent claims may be construed in a manner that would limit our ability to enforce such claims against the defendant and others. Any loss of patent protection could have a material adverse impact on one or more of our product candidates and our business.

Enforcing our intellectual property rights against third parties may also cause such third parties to file other counterclaims against us, which could be costly to defend and could require us to pay substantial damages, cease the sale of certain products or enter into a license agreement and pay royalties (which may not be possible on commercially reasonable terms or at all). Any efforts to enforce our intellectual property rights are also likely to be costly and may divert the efforts of our scientific and management personnel. Any efforts to enforce our intellectual property rights are also likely to be costly, as may well be the case with the Pfizer suit, and may divert the efforts of our scientific and management personnel.

***Intellectual property litigation may lead to unfavorable publicity that harms our reputation and causes the market price of our common stock to decline.***

During the course of any intellectual property litigation, there could be public announcements of the results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our products, programs or intellectual property could be diminished. Accordingly, the market price of our common stock may decline. Such announcements could also harm our reputation or the market for our future products, which could have a material adverse effect on our business.

***Intellectual property rights do not necessarily protect us from 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 compounds that are similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or may in the future exclusively license, which could result in the patent applications not issuing or being invalidated after issuing;
- we might not have been the first to file patent applications covering certain of our inventions, which could result in the patent applications not issuing or being invalidated after issuing;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors; we may obtain patents for certain compounds many years before we obtain marketing approval for products containing such compounds, and because patents have a limited life, which may begin to run prior to the commercial sale of the related product, the commercial value of our patents may be limited;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may fail to develop additional proprietary technologies that are patentable;
- the laws of certain foreign countries may not protect our intellectual property rights to the same extent as the laws of the United States, or we may fail to apply for or obtain adequate intellectual property protection in all the jurisdictions in which we operate; and

- the patents of others may have an adverse effect on our business, for example, by preventing us from marketing one or more of our product candidates for one or more indications.

Any of the aforementioned threats to our competitive advantage could have a material adverse effect on our business.

***Unfavorable outcomes in intellectual property litigation could limit our research and development activities and/or our ability to commercialize certain products.***

If third parties successfully assert their intellectual property rights against us, we might be barred from using certain aspects of our technology or barred from developing and commercializing certain products. Prohibitions against using certain technologies, or prohibitions against commercializing certain products, could be imposed by a court or by a settlement agreement between us and a plaintiff. In addition, if we are unsuccessful in defending against allegations that we have infringed, misappropriated or otherwise violated patent or other intellectual property rights of others, we may be forced to pay substantial damage awards to the plaintiff. There is inevitable uncertainty in any litigation, including intellectual property litigation. There can be no assurance that we would prevail in any intellectual property litigation, even if the case against us is weak or flawed. If litigation leads to an outcome unfavorable to us, we may be required to obtain a license from the intellectual property owner to continue our research and development programs or to market any resulting product. It is possible that the necessary license will not be available to us on commercially acceptable terms, or at all. Alternatively, we may be required to modify or redesign our products to avoid infringing or otherwise violating third-party intellectual property rights. This may not be technically or commercially feasible, may render our products less competitive, or may delay or prevent the entry of our products to the market. Any of the foregoing could limit our research and development activities, our ability to commercialize one or more product candidates, or both.

Most of our competitors are larger than we are and have substantially greater resources. They are, therefore, likely to be able to sustain the costs of complex intellectual property litigation longer than we could. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to conduct our clinical trials, continue our internal research programs, in-license needed technology, or enter into strategic partnerships that would help us bring our product candidates to market. In addition, any future intellectual property litigation, interference or other administrative proceedings will result in additional expense and distraction of our personnel. An adverse outcome in such litigation or proceedings may expose us or any future strategic partners to loss of our proprietary position, expose us to significant liabilities, or require us to seek licenses that may not be available on commercially acceptable terms, if at all, each of which could have a material adverse effect on our business.

***Confidentiality agreements with employees and third parties may not prevent unauthorized disclosure of trade secrets and other proprietary information.***

In addition to patents, we rely on trade secrets, technical know-how and proprietary information concerning our business strategy and product candidates to protect our competitive position in the field of each of our antiviral product candidates and our NASH compounds. In the course of our research and development activities and our business activities, we often rely on confidentiality agreements to protect our proprietary information. Such confidentiality agreements are used, for example, when we talk to vendors of laboratory or clinical development services or potential strategic partners. In addition, each of our employees is required to sign a confidentiality agreement and invention assignment agreement upon joining our company. We take steps to protect our proprietary information, and our confidentiality agreements and invention assignment agreements are carefully drafted to protect our proprietary interests. Nevertheless, there can be no guarantee that an employee or an outside party will not make an unauthorized disclosure of our proprietary confidential information. This might happen intentionally or inadvertently. It is possible that a competitor will make use of such information, and that our competitive position will be compromised, in spite of any legal action we might take against persons making such unauthorized disclosures. In addition, to the extent that our employees, consultants or contractors 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. Trade secrets are difficult to protect. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, business partners or outside scientific collaborators might intentionally or inadvertently disclose our trade secret information to competitors or our trade secrets may otherwise be misappropriated. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States sometimes are less willing than United States courts to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

Our collaborators may have rights to publish data and other information to which we have rights. In addition, we sometimes engage individuals or entities to conduct research relevant to our business. The ability of these individuals or entities to publish or otherwise publicly disclose data and other information generated during the course of their research is subject to certain contractual limitations. These contractual provisions may be insufficient or inadequate to protect our confidential information. If we do not apply for patent protection prior to such publication, or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized, which could adversely affect our business.



***Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.***

As is the case with many other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining, maintaining and enforcing patents in the biopharmaceutical industry involves both technological complexity and legal complexity. Therefore, the process of obtaining, maintaining and enforcing biopharmaceutical patents is costly, time-consuming and inherently uncertain. In addition, recent legislative and judicial developments in the United States and elsewhere have in some cases narrowed the protection afforded to patent owners, made patents more difficult to obtain, or increased the uncertainty regarding the ability to obtain, maintain and enforce patents. For example, Congress recently passed patent reform legislation, and may pass patent reform legislation in the future. The United States Supreme Court has ruled on several patent cases in recent years, and in certain circumstances has narrowed the scope of patent protection available or otherwise weakened the rights of patent owners. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions and actions by the United States Congress, the federal courts, the United States Patent and Trademark Office, and their respective foreign counterparts, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to maintain and enforce our existing patents and patents that we might obtain in the future.

**Risks Related to Our Industry**

***If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.***

We face an inherent risk of product liability as a result of the clinical testing of our product candidates, and we will face an even greater risk if we commercialize any product candidates. For example, we may be sued if any of our product candidates, including any that are developed in combination therapies, allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. There is also risk that third parties we have agreed to indemnify could incur liability. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our product candidates or any resulting products;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- the inability to commercialize our product candidates; and
- a decline in our stock price.

Our inability to obtain and 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. We currently carry product liability insurance covering our clinical studies in the amount of \$15.0 million in the aggregate. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will 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.

***Our internal computer systems, or those of our collaborator, CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of development programs for our product candidates.***

Despite the implementation of security measures, our internal computer systems and those of our collaborators, CROs, and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, pandemics, terrorism, war and telecommunication and electrical failures. Information security risks have significantly increased in recent years and during the COVID-19 pandemic in part due to the proliferation of new technologies, the increased sophistication and activities of organized crime, hackers, terrorists and other external parties, including foreign state actors as well as remote working for many businesses. As cyber threats continue to evolve, we may be required to expend significant additional resources to continue to modify or enhance our protective measures or to investigate and remediate any information security breaches.

While we have not experienced any such 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 independent drug development programs. For example, the loss of clinical trial data from ongoing or future clinical trials for any of our product candidates could result in delays in regulatory approval efforts and significantly increase costs to recover or reproduce the data. Our information security systems are also subject to laws and regulations requiring that we take measures to protect the privacy and security of certain information we gather and use in our business. For example, HIPAA and its implementing regulations impose, among other requirements, certain regulatory and contractual requirements regarding the privacy and security of personal health information. In the European Union, the General Data Protection Regulation, or GDPR, is even more restrictive with respect to all personal information, including information masked by a coding system. In addition to HIPAA and GDPR, numerous other federal and state laws, including, without limitation, state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use, disclosure and storage of personal information. To the extent that any disruption or security breach were to result in a loss of or damage to data or applications, or inappropriate disclosure of confidential or proprietary information or personal health information, we could incur substantial liability, our reputation would be damaged, and the further development of our product candidates could be delayed.

***Our relationships with customers and third-party payors in the United States and elsewhere will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.***

Healthcare providers, physicians and third-party payors in the United States and elsewhere play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal, state and foreign healthcare laws and regulations include the following:

- the federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;
- the federal False Claims Act imposes criminal and civil penalties, including civil whistleblower or *qui tam* actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements under the Patient Protection and Affordable Care Act of 2010 require manufacturers of drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests;
- analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical

industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures; and

- analogous anti-kickback, fraud and abuse and healthcare laws and regulations in foreign countries.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, which could have a material adverse effect on our business. If any of the physicians or other providers or entities with whom we expect to do business, including our collaborators, are found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs, which could also materially affect our business.

## **Risks Related to Our Common Stock**

***Our stock price has been, and is likely to continue to be, volatile, and thus our stockholders could incur substantial losses.***

Our stock price has been volatile and could be subject to wide fluctuations in response to various factors, many of which are beyond our control. From June 30, 2016 through September 30, 2022, the daily closing price of our common stock on the NASDAQ Global Select Market has ranged from \$21.00 to \$126.37. The stock market in general and the market for biopharmaceutical companies, and for those developing potential therapies for viral infections and liver diseases in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies, which in some cases has been exacerbated by the COVID-19 pandemic. As a result of this volatility, you may not be able to sell your holdings of our common stock at or above your purchase price, if at all. The market price for our common stock may be influenced by many factors, including:

- results from or delays of clinical trials of our product candidates, as well as results of regulatory reviews relating to the approval of our product candidates;
- actions by AbbVie regarding the MAVYRET/MAVIRET regimen, including announcements regarding regulatory or commercial developments;
- market expectations about and response to the levels of sales or scripts achieved by, or the announced prices or discounts for, AbbVie's MAVYRET/MAVIRET regimen or competitive HCV drugs;
- failure of AbbVie's MAVYRET/MAVIRET regimen to maintain its sales levels;
- the results of our efforts to discover or develop additional product candidates;
- new products, product candidates or new uses for existing products or technologies introduced or announced by our competitors and the timing of these introductions or announcements;
- our dependence on third parties, including our collaborators, CROs, manufacturers, clinical trial sponsors and clinical investigators;
- regulatory, political or legal developments in the United States or other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key scientific or management personnel;
- our ability to commercialize our product candidates we develop independently, if approved;
- the level of expenses related to any of our product candidates or clinical development programs;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- period-to-period variations in our financial results or those of companies that are perceived to be similar to us;
- sales of common stock by us or our stockholders in the future, as well as the overall trading volume of our common stock;
- changes in the structure of healthcare payment systems or other actions that affect the effective reimbursement rates for treatment regimens containing our products or for competitive regimens;

- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies; and
- the other factors described in this “Risk Factors” section.

***Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, 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 corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which they might otherwise receive a premium for their shares.

These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified or staggered board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- provide that the state courts or, in certain circumstances, the federal courts, in Delaware shall be the sole and exclusive forum for certain actions involving us, our directors, officers, employees and stockholders;
- provide our board of directors with the authority to designate the terms of and issue a new series of preferred stock without stockholder approval, which could be used to institute a “poison pill” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 66 2/3% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibit a person who owns 15% or more 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. Any provision in our corporate charter or our bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock and could also affect the price that some investors are willing to pay for our common stock.

***Our employment agreements with our executive officers may require us to pay severance benefits to any of those persons who are terminated in connection with a change of control of us, which could harm our financial condition or results.***

Our executive officers are parties to employment agreements that provide for aggregate cash payments of up to approximately \$6.0 million for severance and other non-equity-based benefits in the event of a termination of employment in connection with a change of control of our company. In addition, based on the closing price of our common stock of \$51.87 per common share as of September 30, 2022, the aggregate intrinsic value of unvested stock options and other equity awards subject to accelerated vesting upon these events was \$18.0 million. The accelerated vesting of awards options could result in dilution to our stockholders and harm the market price of our common stock. The payment of these severance benefits could harm our company’s financial condition and results. In addition, these potential severance payments may discourage or prevent third parties from seeking a business combination with us.



***Because we do not anticipate paying cash dividends on our common stock for the foreseeable future, investors in our common stock may never receive a return on their investment.***

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock for the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations.

Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not invest in our common stock.

***A sale of a substantial number of shares of our common stock in the public market could cause the market price of our common stock to drop significantly, even if our business is doing well.***

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of September 30, 2022 we had 20.8 million shares of common stock outstanding. In addition, as of September 30, 2022, we had 4.0 million and 0.4 million shares of common stock that are subject to outstanding options and restricted stock unit awards, respectively, under our outstanding equity plans eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, and Rule 144 under the Securities Act. If these additional shares of common stock are sold, or it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

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

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. If those analysts are unable to predict accurately the demand and net sales of AbbVie's HCV regimens, that could result in our reported revenues and earnings being lower than the so-called "market consensus" of our projected revenues, which could negatively affect our stock price. In addition, if too few securities or industry analysts cover our company, the trading price for our stock would likely be negatively impacted. In the event that one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

## **General Risk Factors**

***If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.***

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials or our or third parties' disposal of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

We may incur substantial costs to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

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

***Our insurance policies are expensive and only protect us from specified business risks, which will leave us exposed to significant uninsured liabilities.***

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, employment practices liability, property, auto, workers' compensation, cybersecurity, products liability and directors' and officers' insurance. We do not know, however, if we have adequate levels of coverage for any liability we may incur, or whether we will always be able to continue to maintain such insurance. Any significant uninsured liability may require us to make

substantial payments, which would adversely affect our financial position and results of operations. Furthermore, any increase in the volatility of our stock price, or changes in the insurance market generally, may result in us being required to pay substantially higher premiums for our directors' and officers' liability insurance than those to which we were previously subject and may even cause one or more of our underwriters to be unwilling to insure us.

***If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.***

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement newly required or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations. In addition, any failure to maintain effective internal control as a result of shutdowns during the global COVID-19 pandemic could result in deficiencies in internal control. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act of 2002, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock.

***Our information technology systems, or those used by our CROs or other contractors or consultants, may fail or suffer other breakdowns, cyber-attacks, or information security breaches, which could adversely affect our business.***

We are increasingly dependent upon information technology systems, infrastructure, and data to operate our business. We also rely on third party vendors and their information technology systems. Despite the implementation of security measures, our recovery systems, security protocols, network protection mechanisms, and other security measures and those of our current or future CROs or other contractors and consultants are vulnerable to system failure, interruption, compromise, or damage from data corruption, breakdown, computer hacking, malicious code (such as computer viruses or worms), fraudulent activity, employee misconduct, theft, or error, denial-of-service attacks, telecommunication, and electrical failures, natural disasters, public health epidemics, such as the COVID-19 pandemic, cyber-attacks by sophisticated nation-state and nation-state supported actors, or other system attacks, disruption, or accidents. We receive, generate and store significant and increasing volumes of personal health data and other confidential and proprietary information. There can be no assurance that we, or our collaborators, CROs, third-party vendors, contractors and consultants, will be successful in efforts to detect, prevent, protect against or fully recover systems or data from all breakdowns, service interruptions, attacks or breaches.

The costs to respond to a security breach and/or to mitigate any security vulnerabilities that may be identified could be significant, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service, negative publicity, and other harm to our business and our competitive position. Remediation of any potential security breach may involve significant time, resources, and expenses. Despite our best efforts, our network security and data recovery measures and those of our vendors may still not be adequate to protect against such security breaches and disruptions, which could cause harm to our business, financial condition and results of operations.

Any cybersecurity incident could adversely affect our business, by leading to, for example, the loss of confidential information or other intellectual property, demands for ransom or other forms of blackmail or the unauthorized disclosure of personal, confidential or proprietary information of our employees, clinical trial participants, customers and others. We could be subject to regulatory actions taken by governmental authorities, litigation under laws that protect the privacy and security of personal information, or other forms of legal proceedings, which could result in significant investigations, liabilities or penalties.

We may not have adequate insurance coverage for security incidents or breaches. The successful assertion of one or more large claims against us that exceeds our available insurance coverage, or results in changes to our insurance policies (including premium increases or the imposition of large deductible or co-insurance requirements), could have an adverse effect on our business. In addition, we cannot be sure that our existing insurance coverage and coverage for errors and omissions will continue to be available on acceptable terms or that our insurers will not deny coverage as to any future claim.

***Use of social media could give rise to liability or reputational harm.***

We and our employees use social media to communicate externally. There is risk that the use of social media by us or our employees to communicate about our product candidates or business may give rise to 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.

**ITEM 1B. UNRESOLVED STAFF COMMENTS**

None.

**ITEM 2. PROPERTIES**

Our corporate headquarters is located in Watertown, Massachusetts, where we lease approximately 49,000 square feet of office and laboratory space under the 500 Arsenal Street lease agreement that expires on September 1, 2027. In May 2022, we entered into a new lease agreement for approximately 73,000 square feet of laboratory and office space in Watertown, Massachusetts, at a to-be-constructed facility located at Arsenal on the Charles. We expect to gain access to the facility in October 2023 to construct tenant improvements. In conjunction with the new lease agreement at Arsenal on the Charles, we amended the 500 Arsenal Street lease agreement to shorten the term of the lease from September 2027 to the date when the Arsenal on the Charles facility is completed and ready for the Company's occupancy. We also lease approximately 38,000 square feet of additional office space located in Watertown, Massachusetts. The term of this lease expires on June 1, 2034.

**ITEM 3. LEGAL PROCEEDINGS**

Information with respect to legal proceedings is included in Note 12 of the Notes to Consolidated Financial Statements contained in Part II, Item 8 of this Annual Report on Form 10-K, which is incorporated herein by reference.

**ITEM 4. MINE SAFETY DISCLOSURES**

Not applicable.

## PART II

### ITEM 5. MARKET FOR THE COMPANY'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

#### Market and Stockholder Information

Our common stock has been listed on The NASDAQ Global Select Market under the symbol “ENTA” since March 21, 2013. The following table shows the high and low sales price for our common stock as reported by The NASDAQ Global Select Market for the quarterly periods in the fiscal years ended September 30, 2022 and 2021:

	Fiscal 2022	
	High	Low
First Quarter	\$ 102.00	\$ 57.21
Second Quarter	\$ 75.28	\$ 54.42
Third Quarter	\$ 79.50	\$ 37.59
Fourth Quarter	\$ 76.36	\$ 47.20

	Fiscal 2021	
	High	Low
First Quarter	\$ 47.47	\$ 41.16
Second Quarter	\$ 54.95	\$ 41.69
Third Quarter	\$ 53.11	\$ 43.76
Fourth Quarter	\$ 58.65	\$ 41.02

As of November 14, 2022 there were 18 stockholders of record of our common stock, which excludes stockholders whose shares were held in nominee or street name by brokers.

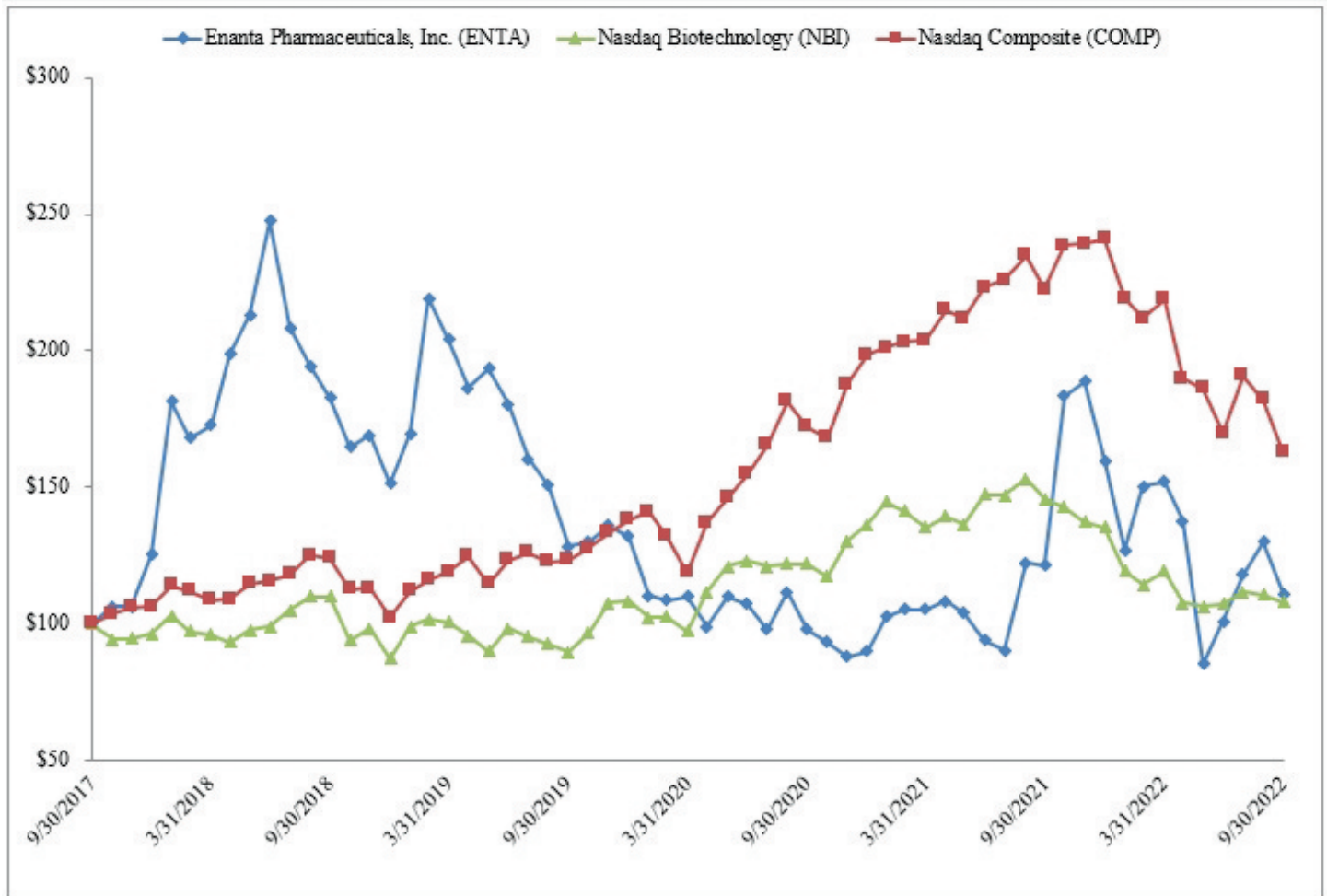
We have never declared or paid cash dividends on our common stock, and we do not expect to declare or pay any cash dividends for the foreseeable future.



### Performance Graph<sup>(1)</sup>

The following graph shows a comparison from September 30, 2017 through September 30, 2022 of cumulative total return on assumed investments of \$100.00 in cash in each of our common stock, the NASDAQ Composite Index and the NASDAQ Biotechnology Index. Such returns are based on historical results and are not intended to suggest future performance. Data for the NASDAQ Composite Index and the NASDAQ Biotechnology Index assume reinvestment of dividends.

#### COMPARISON OF FIVE YEARS CUMULATIVE TOTAL RETURN Among Enanta Pharmaceuticals, Inc., the NASDAQ Composite Index, and the NASDAQ Biotechnology Index



- <sup>(1)</sup> This performance graph shall not be deemed to be “soliciting material” or to be “filed” with the SEC for purposes of Section 18 of the Securities and Exchange Act of 1934, as amended, or otherwise subject to the liabilities under that Section, and shall not be deemed incorporated by reference into any filing of Enanta Pharmaceuticals, Inc. under the Securities Act of 1933, as amended.

**ITEM 6. [RESERVED]**

## ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

*You should read the following discussion and analysis of financial condition and results of operations together with our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This discussion and other parts of this Annual Report on Form 10-K contain forward-looking statements that involve risks and uncertainties, such as statements regarding our plans, objectives, expectations, intentions, and projections. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the "Risk Factors" section of this Annual Report on Form 10-K.*

### Overview

We are a biotechnology company that uses our robust, chemistry-driven approach and drug discovery capabilities to become a leader in the discovery and development of small molecule drugs, with an emphasis on treatments for viral infections. We discovered glecaprevir, the second of two protease inhibitors discovered and developed through our collaboration with AbbVie for the treatment of chronic infection with hepatitis C virus, or HCV. Glecaprevir is co-formulated as part of AbbVie's leading brand of direct-acting antiviral, or DAA, combination treatment for HCV, which is marketed under the tradenames MAVYRET® (U.S.) and MAVIRET® (ex-U.S.) (glecaprevir/pibrentasvir). Our royalties from our AbbVie collaboration provide us funding to support our wholly-owned research and development programs, which are primarily focused on the following disease targets:

- Respiratory syncytial virus, or RSV, the most common cause of bronchiolitis and pneumonia in young children and a significant cause of respiratory illness in older adults, with estimates suggesting that on average each year RSV leads to 3 million hospitalizations globally in children under 5 years old and 177,000 hospitalizations in the U.S. in adults over the age of 65;
- SARS-CoV-2, the virus that causes COVID-19, as well as other coronaviruses, with estimates suggesting that COVID-19 has caused over 240,000 deaths and over 1.7 million hospitalizations in the U.S. in 2022 through October 29, with comparable, or at least significant, impact in other major populations of the world and with new variants still emerging;
- Hepatitis B virus, or HBV, the most prevalent chronic hepatitis, which is estimated by the World Health Organization to affect close to 300 million individuals worldwide; and
- Human metapneumovirus, or hMPV, an important, relatively recently identified cause of respiratory tract infections, particularly in children, the elderly and immunocompromised individuals, with symptoms similar to RSV.

We had \$278.5 million in cash, cash equivalents and short-term and long-term marketable securities at September 30, 2022. In fiscal 2022, we earned \$86.2 million in product royalties on AbbVie's net sales of its HCV regimens. We expect cash flows from our continuing HCV royalties and our existing financial resources will allow us to continue to fund our wholly-owned research and development programs into approximately the fourth quarter of fiscal 2024.

### Our Wholly-Owned Programs

Our primary wholly-owned research and development programs are in virology, namely RSV, SARS-CoV-2, HBV and hMPV:

- **RSV:** We have a clinical stage program for RSV, with two compounds in clinical trials – EDP-938 and EDP-323. EDP-938, which has Fast Track designation from the U.S. Food and Drug Administration, or FDA, is a potent N-protein inhibitor of activity of both major subgroups of RSV, referred to as RSV-A and RSV-B. It has been investigated in a Phase 2a challenge study and is currently in three ongoing Phase 2 studies, each in a different patient population. In addition, we recently announced the initiation of a Phase 1 clinical study of EDP-323, an inhibitor of the RSV L-protein.
  - o ***EDP-938 - N-protein Inhibitor Candidate:*** We have studied EDP-938 in two Phase 2 studies that were designed to be proof-of-concept and exploratory to understand better viral response in the context of RSV infection. These studies were conducted in otherwise healthy adults. The first study was the challenge study, which was reported out in mid-2019. The second study, known as RSVP, was designed to confirm the challenge study findings in an adult outpatient population with community-acquired RSV infection to provide additional information on symptom alleviation and viral load decline. In May 2022, we announced topline results for RSVP, noting that EDP-938 did not meet the primary endpoint of reduction in total symptom score compared to placebo, or the secondary antiviral endpoints. However, a statistically significant difference in the number of subjects achieving undetectable RSV RNA at the end of treatment at Day 5 was observed with EDP-938 compared to placebo ( $p=0.033$ ). Further, EDP-938 demonstrated a favorable safety profile, consistent with that observed in approximately 500 subjects exposed to EDP-938 to date. Based on the growing safety profile of EDP-938 and differences in the range of the course of RSV infection in higher risk populations, which have always been our target populations, EDP-938 merits continued study. We believe that EDP-938 continues to have the greatest potential to show optimal efficacy in high-risk

populations, as these patients have reduced RSV immunity, which manifests in a higher and longer duration of viral load and greater disease severity, allowing a bigger window to realize the full potential of EDP-938. We are continuing to evaluate EDP-938 in high-risk populations in the following ongoing and planned clinical studies, including pediatric patients, adult hematopoietic stem cell recipients and high-risk adults, all of which have significant unmet need:

- RSVPEDs: RSVPEDs is a Phase 2 study in pediatric patients. This dose-ranging, randomized, double-blind, placebo-controlled study, will evaluate multiple ascending doses in up to four age cohorts to determine safety, tolerability, and pharmacokinetics, as well as a second part evaluating the selected dose for antiviral activity.
- RSVTx: RSVTx is a Phase 2b study in adult hematopoietic cell transplant recipients with acute RSV infection and symptoms of upper respiratory tract infection. We plan to enroll approximately 200 adult subjects 18 to 75 years of age, within 72 hours of symptom onset, who will receive EDP-938 or placebo for 21 days and will be monitored for the incidence of lower respiratory tract complications within 28 days of enrollment.
- RSVHR: On October 3, 2022, we announced the initiation of a Phase 2b study called RSVHR in high-risk adults, including those who are older than 65 years of age and those who have asthma, chronic obstructive pulmonary disease, or COPD, or congestive heart failure. Approximately 180 patients will be treated with 800 mg of EDP-938 or placebo for five days and evaluated for 28 days thereafter. The primary endpoint of the study is time to resolution of RSV lower respiratory tract disease symptoms.
- The prevalence of RSV has not been following any normal seasonal pattern since the COVID-19 pandemic began. The future incidence and timing of RSV infections remain highly unpredictable and thus may continue to impact enrollment in our ongoing Phase 2 RSV trials.
- EDP-323 - L-protein Inhibitor Candidate: Our newest clinical candidate for RSV is a novel oral, direct-acting antiviral selectively targeting the RSV L-protein, a viral RNA-dependent RNA polymerase enzyme that contains multiple enzymatic activities required for RSV replication. EDP-323 has shown nanomolar potency against RSV-A and RSV-B *in vitro* and is not expected to have cross-resistance to other classes of inhibitors. EDP-323 has the potential to be used alone or in combination with other RSV mechanisms, such as EDP-938, to broaden the treatment window or addressable patient populations. We initiated a Phase 1 clinical study of EDP-323 in October 2022.
- COVID-19: We have been leveraging our expertise in developing protease inhibitors to discover new compounds specifically designed to target the SARS-CoV-2 virus and potentially other coronaviruses.
  - EDP-235 – Protease Inhibitor Candidate – Our lead clinical candidate for COVID-19, EDP-235, is an oral inhibitor of coronavirus 3CL protease, also referred to as 3CLpro or the main coronavirus protease, or Mpro, which has been granted Fast Track designation by the FDA. In addition to SARS-CoV-2, EDP-235 has potent antiviral activity against other human coronaviruses, enabling the potential for a pan-coronavirus treatment, including possibly coronaviruses that may infect human populations in the future.
    - Phase 1 Study – In July 2022, we completed a Phase 1 study and reported positive topline results. This first-in-human, randomized, double-blind, placebo-controlled study enrolled healthy volunteers to evaluate the safety, tolerability, and pharmacokinetics, or PK, of oral EDP-235 in single ascending doses and multiple ascending doses for seven days, and the effect of food. Data from the Phase 1 study demonstrated EDP-235 was generally safe and well-tolerated up to 400 mg for seven days with strong exposure multiples over the EC<sub>90</sub>, which is a measure of potency, specifically the concentration of drug that results in 90% inhibition of viral replication *in vitro*. EDP-235 200 mg taken once daily with food resulted in mean trough plasma levels at steady state that were 3-fold and 7-fold over the plasma-protein-adjusted EC<sub>90</sub> for the tested Alpha variant and Omicron variant, respectively, while 400 mg resulted in levels that were 6-fold and 13-fold over the plasma-protein-adjusted EC<sub>90</sub> for the respective variants. These target exposure multiples were achieved without the need for ritonavir boosting and its associated drug-drug interactions. EDP-235 is projected to have four times higher drug levels in lung tissue compared to plasma, which would be expected to drive the 400 mg multiples to 28-fold and 52-fold for the respective variants. Adverse events were infrequent and mild.
    - Phase 2 Study – In November 2022, we initiated SPRINT (SARS-Cov-2 **P**rotease **I**nhibitor **T**reatment), a Phase 2 clinical trial of EDP-235 in non-hospitalized, symptomatic adults with mild or moderate COVID-19. This randomized, double-blind, placebo-controlled study is designed to evaluate the safety, tolerability and antiviral activity of 200 mg and 400 mg once-daily doses of EDP-235 compared to placebo. The study will enroll approximately 200 non-hospitalized, symptomatic patients with mild to moderate COVID-19 who are not at increased risk for developing severe disease. Patients will be eligible to participate if they have had

symptoms for five days or less and have not received a SARS-CoV-2 vaccine or been infected with SARS-CoV-2 within 90 days of enrollment. Patients will receive EDP-235 orally with food at a dose of 200 mg or 400 mg or placebo once daily for five days. The primary objective of the study includes evaluation of safety and tolerability, and secondary objectives include pharmacokinetics and multiple virology measures to guide dose selection for other trials.

- o We are also researching additional compounds that might be eligible to be designated for clinical development for SARS-CoV-2.
- **HBV:** Our lead clinical candidate for the treatment of chronic infection with hepatitis B virus, or HBV, is EDP-514, a core inhibitor that displays potent anti-HBV activity *in vitro* at multiple points in the HBV lifecycle. Our goal is to develop a combination therapy approach, including existing approved treatments such as a nucleoside reverse transcriptase inhibitor, or NUC, with EDP-514 and one or more other mechanisms, which could lead to a functional cure for patients with chronic HBV infection. We are in the process of seeking other compounds that could be developed with EDP-514 for such a treatment regimen.
- o **EDP-514 - Core Inhibitor Candidate** - In June 2022, final data from two of our Phase 1b studies of EDP-514 were presented at The International Liver Congress™ 2022. EDP-514, which has Fast Track designation from the FDA, has been shown to be safe and potent in two different chronic HBV patient populations – those who have a high viral load, whom we refer to as viremic patients, and those who are on a treatment with a nucleoside reverse transcriptase inhibitor, whom we refer to as NUC-suppressed patients. Based on these data, we remain convinced that EDP-514 has the potential to be a best-in-class core inhibitor for HBV.
- **hMPV:** Human metapneumovirus, or hMPV, a virus that is a significant cause of respiratory tract infections, or RTIs, particularly in children, the elderly and immunocompromised individuals. It is the second most common cause of lower respiratory tract infections in children, with symptoms similar to RSV. The viral structure and lifecycle of hMPV are also similar to RSV. We have been optimizing nanomolar inhibitor leads against hMPV and are working toward selecting our first development candidate for this indication in 2023.

We have utilized our internal chemistry and drug discovery capabilities to generate all of our development-stage programs. We continue to invest substantial resources in research programs to discover back-up compounds as well as new compounds targeting different mechanisms of action, both in our disease areas of focus as well as potentially in other disease areas.

### ***Our Royalty Revenue Collaboration***

Our royalty revenue is generated through our Collaborative Development and License Agreement with AbbVie, under which we have discovered and out-licensed to AbbVie two protease inhibitor compounds that have been clinically tested, manufactured, and commercialized by AbbVie as part of its combination regimens for HCV.

Glecaprevir is the HCV protease inhibitor we discovered that was developed by AbbVie in a fixed-dose combination with its NS5A inhibitor, pibrentasvir, for the treatment of chronic HCV. This patented combination, currently marketed under the brand names MAVYRET® (U.S.) and MAVIRET® (ex-U.S.), is referred to in this report as MAVYRET/MAVIRET. The first protease inhibitor developed through this collaboration, paritaprevir, is part of AbbVie's initial HCV regimens, which have been almost entirely replaced by MAVYRET/MAVIRET. Since August 2017, substantially all of our royalty revenue has been derived from AbbVie's net sales of MAVYRET/MAVIRET. Our ongoing royalty revenues from this regimen consist of annually tiered, double-digit, per-product royalties on 50% of the calendar year net sales of the 2-DAA glecaprevir/pibrentasvir combination in MAVYRET/MAVIRET. The annual royalty tiers return to the lowest tier for sales on and after each January 1.

### **COVID-19 Update**

The current COVID-19 pandemic has presented substantial challenges for public health and economies around the world, and it is affecting our clinical trials, our royalty revenues received from AbbVie, and our business operations. The full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition will depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning COVID-19 and public health actions taken to contain it and roll out vaccinations worldwide, as well as the cumulative economic impact of all of these factors. Additionally, as new, more infectious variants emerge, such as the Omicron variants, it is possible that the impact of the pandemic on our business may continue or change.

We are continuing to assess and manage the potential impact of the COVID-19 pandemic on our business and operations, including our expenses, clinical trials and royalty revenue. While the majority of our employees were working from home during the first 18 months of the pandemic, as we prepare to transition back to working on site, the majority of our employees are now working hybrid schedules while our scientific personnel are working full-time in our laboratories.



Our third-party contract manufacturing partners continue to operate at or near normal levels producing drug substance and drug product for our research and clinical development programs, so we currently do not anticipate any material interruptions in our supply chain, but it is possible that may change. In addition, the mitigation steps to manage the COVID-19 pandemic in the past two years have suppressed the global incidence of RSV and respiratory illnesses other than COVID-19, which has adversely affected enrollment in our RSV studies. We also continue to experience a variety of more minor interruptions and complications in our clinical trials, such as limitations in clinical trial supplies other than drug product, as well as local changes in COVID-19 impacts at individual trial sites. While our ongoing trials are proceeding, it is unclear what further impact, if any, the COVID-19 pandemic may have on the timeline for enrollment and/or completion of all or any of our clinical trials.

Regarding our royalty revenue, we continued to report lower royalty revenue during fiscal 2022 as compared to periods ending before March 2020 due to the worldwide impact of the COVID-19 pandemic. The pandemic resulted in a decline in patient volumes, HCV diagnoses, HCV prescriptions and sales of MAVYRET/MAVIRET.

While the evolving impact of COVID-19 will likely continue to affect aspects of our business, including those described above, we remain capable of funding our research and development programs into approximately the fourth quarter of fiscal 2024 with the current level of royalty revenue and our existing cash, cash equivalents and short-term and long-term marketable securities, which totaled \$278.5 million at September 30, 2022.

Please see Item 1A “Risk Factors” in this Form 10-K for additional discussion of risks and potential risks of the COVID-19 pandemic on our business, results of operations and financial condition.

## Financial Operations Overview

We are currently funding all research and development for our wholly-owned programs, which are targeted toward the discovery and development of novel compounds with an emphasis on treatments for viral infections. As of November 2022, we are conducting three Phase 2 studies and one Phase 1 study in our RSV program and one Phase 2 study in our SARS-CoV-2 program. We are also progressing other compounds into preclinical development.

During fiscal 2022, our business has been impacted by the COVID-19 pandemic. Specifically, AbbVie continues to report lower HCV revenues as a result of lower treated patient volumes. In addition, the prevalence of RSV has not been following any normal seasonal pattern since the COVID-19 pandemic began, and we continued to experience slower enrollment in the clinical studies in our RSV program as a result of suppression of the incidence of respiratory illnesses globally (other than COVID-19) due to mitigation measures intended to suppress SARS-CoV-2.

As a result of the timing of our clinical and preclinical development programs, we expect our research and development expenses to fluctuate from period to period. However, in the coming years, we expect our research and development expenses generally to increase as our wholly-owned programs advance.

We are funding our operations primarily through royalty payments received under our collaboration agreement with AbbVie and our existing cash, cash equivalents, and short-term and long-term marketable securities. Our revenue is currently dependent on royalty payments we receive from AbbVie on its sales of MAVYRET/MAVIRET. Absent a significant increase in the level of AbbVie’s MAVYRET/MAVIRET sales that generate our royalty revenue, and given the planned levels of our future expenditures for the advancement of our internally developed compounds, we expect to continue to have net losses in fiscal 2023.

## Revenue

Our revenue is derived from our collaboration agreement with AbbVie and AbbVie’s sales of MAVYRET/MAVIRET, an 8-week treatment regimen for chronic HCV.

The following table is a summary of revenue recognized for the years ended September 30, 2022, 2021, and 2020:

	Years Ended September 30,		
	2022	2021	2020
	(in thousands)		
AbbVie agreement:			
Royalties	\$ 86,160	\$ 97,074	\$ 122,473
Total revenue	<u>\$ 86,160</u>	<u>\$ 97,074</u>	<u>\$ 122,473</u>

## AbbVie Agreement

We currently receive annually tiered, double-digit royalties on our protease inhibitor product glecaprevir included in AbbVie’s net sales of MAVYRET/MAVIRET. Under the terms of our AbbVie agreement, as amended in October 2014, 50% of AbbVie’s net sales of MAVYRET/MAVIRET are allocated to glecaprevir. Beginning with each January 1, the cumulative net sales of

MAVYRET/MAVIRET start at zero for purposes of calculating the tiered royalties. For detail regarding the royalty tiers under our AbbVie agreement, see Note 7 in Notes to Consolidated Financial Statements of this report, which is incorporated herein by this reference.

### Internal Programs

As our internal product candidates are currently in Phase 1 or Phase 2 clinical development, we have not generated any revenue from our own product sales and do not expect to generate any revenue from product sales derived from these product candidates for at least the next several years.

### Operating Expenses

The following table summarizes our operating expenses for the years ended September 30, 2022, 2021, and 2020:

	Years Ended September 30,		
	2022	2021 (in thousands)	2020
Research and development	\$ 164,522	\$ 174,111	\$ 136,756
General and administrative	45,482	32,536	27,356
Total operating expenses	<u>\$ 210,004</u>	<u>\$ 206,647</u>	<u>\$ 164,112</u>

### Research and Development Expenses

Research and development expenses consist of costs incurred to conduct basic research, such as the discovery and development of novel small molecules as therapeutics, as well as any external expenses of preclinical and clinical development activities. We expense all costs of research and development as incurred. These expenses consist primarily of:

- personnel costs, including salaries, related benefits and stock-based compensation for employees engaged in scientific research and development functions;
- third-party contract costs relating to research, formulation, manufacturing, preclinical study and clinical trial activities;
- laboratory consumables;
- allocated facility-related costs; and
- third-party license fees.

Project-specific expenses reflect costs directly attributable to our clinical development candidates and preclinical candidates nominated and selected for further development. Remaining research and development expenses are reflected in research and drug discovery, which represents early-stage drug discovery programs. At any given time, we typically have several active early-stage research and drug discovery projects. Our internal resources, employees and infrastructure are not directly tied to any individual research or drug discovery project and are typically deployed across multiple projects. As such, we do not report information regarding costs incurred for our early-stage research and drug discovery programs on a project-specific basis. We expect that our research and development expenses will increase in the future as we advance our research and development programs. To date we have not identified any significant impact of inflation on spending in research and development, but it is uncertain whether there will be inflationary impacts in future periods.

Our research and drug discovery and development programs are at early stages; therefore, the successful development of our product candidates is highly uncertain and may not result in approved products. Completion dates and completion costs can vary significantly for each product candidate and are difficult to predict. Given the uncertainty associated with clinical trial enrollments, particularly in the context of the COVID-19 pandemic, and the risks inherent in the development process, we are unable to determine the duration and completion costs of the current or future clinical trials of our product candidates or if, or to what extent, we will generate revenue from the commercialization and sale of any of our product candidates. We anticipate that we will make determinations as to which development programs to pursue and how much funding to direct to each program on an ongoing basis in response to the preclinical and clinical success and prospects of each product candidate, as well as ongoing assessments of the commercial potential of each product candidate.

### General and Administrative Expenses

General and administrative expenses consist primarily of personnel costs, which include salaries, related benefits and stock-based compensation, of our executive, finance, business and corporate development and other administrative functions. General and administrative expenses also include travel expenses, allocated facility-related costs not otherwise included in research and

development expenses, directors' and officers' liability insurance premiums, professional fees for auditing, tax, and legal services, and patent expenses.

We expect that general and administrative expenses will continue to increase in the future primarily due to the ongoing expansion of our operating activities in support of our own research and development programs, as well as our patent litigation seeking damages for infringement of one of our COVID-19 patents. To date we have not experienced a significant impact of inflation on spending in general and administrative, but we anticipate inflation may impact future periods.

#### ***Other Income (Expense)***

Other income (expense) consists of interest and investment income, net and the change in fair value of our outstanding Series 1 nonconvertible preferred stock. Interest income consists of interest earned on our cash equivalents and short-term and long-term marketable securities balances and interest earned for any refunds received from tax authorities. Investment income consists of the amortization or accretion of any purchased premium or discount, respectively, on our short-term and long-term marketable securities. The change in fair value of our Series 1 nonconvertible preferred stock relates to the remeasurement of these financial instruments from period to period as these instruments may require a transfer of assets because of the liquidation preference features of the underlying instrument.

#### ***Income Tax Benefit (Expense)***

Income tax benefit for the year ended September 30, 2022 is the result of the release of a state tax reserve. Income tax benefit (expense) for the years ended September 30, 2021 and 2020 is the result of federal and state taxes generated from our domestic operations or the benefit of tax refunds due as a result of tax losses generated in the period which were able to be carried back to prior years under the Coronavirus Aid, Relief and Economic Security Act, or CARES Act. The tax refunds provided by the CARES Act are no longer available to us for periods after September 30, 2021.

Income tax benefit (expense) is based on our best estimate of applicable income tax rates, net research and development tax credits, net operating loss carrybacks, changes in valuation allowance estimates and deferred income taxes.

#### ***Critical Accounting Policies***

Our consolidated financial statements are prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amount of assets, liabilities, equity, revenue, costs and expenses, and related disclosures. We believe that the estimates and assumptions involved in the accounting policies described below may have the greatest potential impact on our consolidated financial statements and, therefore, consider these to be our critical accounting policies. We evaluate our estimates and assumptions on an ongoing basis. Actual results may differ from these estimates under different assumptions and conditions. See also Note 2 to the consolidated financial statements included elsewhere in this Annual Report on Form 10-K for information about these critical accounting policies as well as a description of our other significant accounting policies.

## Research and Development and Pharmaceutical Drug Manufacturing Accruals

We have entered into various contracts with third parties to perform research and development and pharmaceutical drug manufacturing. These include contracts with contract research organizations, or CROs, clinical manufacturing organizations, or CMOs, testing laboratories, research hospitals and not-for-profit organizations and other entities to support our research and development activities. We expense the cost of each contract as the work is performed. When billing terms under these contracts do not coincide with the timing of when the work is performed, we are required to make estimates of our outstanding obligations to those third parties as of period-end. Our accrual estimates are based on a number of factors, including our knowledge of the research and development programs and pharmaceutical drug manufacturing activities and associated timelines, invoicing to date, and the provisions in the contract. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from our estimates.

## Results of Operations

	Years Ended September 30,		
	2022	2021	2020
	(in thousands)		
Revenue	\$ 86,160	\$ 97,074	\$ 122,473
Research and development	164,522	174,111	136,756
General and administrative	45,482	32,536	27,356
Other income (expense):			
Interest and investment income, net	1,573	2,021	6,471
Change in fair value of Series 1 nonconvertible preferred stock	83	(27)	149
Income tax benefit (expense)	433	28,583	(1,149)
Net loss	<u>\$ (121,755)</u>	<u>\$ (78,996)</u>	<u>\$ (36,168)</u>

## Comparison of the Years Ended September 30, 2022 and 2021

**Revenue.** We recognized revenue of \$86.2 million and \$97.1 million during the years ended September 30, 2022 and 2021, respectively. The decrease in revenue year-over-year was due to AbbVie's lower reported HCV sales in 2022, as compared to 2021. Our weighted average royalty rate on the portion of AbbVie's sales allocable to our protease inhibitor products was approximately 11% in both fiscal 2022 and 2021.

Our royalty revenues eligible to be earned in the future will depend on AbbVie's HCV market share, the pricing of the MAVYRET/MAVIRET regimen and the number of patients treated. In addition, at the beginning of each calendar year (the second quarter of our fiscal year), our royalty rate resets to the lowest tier for each of our royalty-bearing products licensed to AbbVie. (See Note 7 to our consolidated financial statements for further details on our royalty rate tier.)

## Research and development expenses.

	Years Ended September 30,	
	2022	2021
	(in thousands)	
R&D programs:		
Virology	\$ 144,344	\$ 127,488
Liver disease (non-viral)	17,658	43,908
Other	2,520	2,715
Total research and development expenses	<u>\$ 164,522</u>	<u>\$ 174,111</u>

Research and development expenses decreased by \$9.6 million for the year ended September 30, 2022, as compared to the same period in 2021. While we incurred increased costs of \$16.9 million in our virology program, costs in our non-viral liver disease program decreased by \$26.3 million from fiscal 2021 to fiscal 2022 as we wound down our non-alcoholic steatohepatitis, or NASH, program, which is now substantially complete. Increased costs in our virology program were primarily due to an increase in manufacturing and clinical trial costs due to the timing and scope of clinical trials. For our virology program, we had three Phase 2 studies of EDP-938 in RSV, one Phase 1 study of EDP-235 in our COVID-19 program, which was initiated during the second quarter of 2022, and a Phase 1a study of an HBV RNA destabilizer that was discontinued in November 2021. In the prior year, we had two Phase 1b studies of EDP-514 in chronic HBV, as well as three Phase 2 studies of EDP-938 in RSV, including the expanded RSVP study, which was ongoing in 2021, and the Phase 1a study of an HBV RNA destabilizer.



We expect our research and development expenses will increase in the future as we conduct more clinical development activities.

**General and administrative expenses.** General and administrative expenses increased to \$45.5 million for the year ended September 30, 2022, as compared to \$32.5 million for the same period in 2021. The increase was primarily due to increases in headcount and stock-based compensation expense to support our research and development operations.

We expect our general and administrative expenses will continue to increase in the future as our operations grow to support further research and development.

**Other income (expense).** Changes in components of other income (expense) were as follows:

*Interest and investment income, net.* Interest and investment income, net decreased by \$0.4 million for the year ended September 30, 2022, as compared to the same period in 2021, primarily due to lower invested cash balances.

**Income tax benefit (expense).** We recorded income tax benefits of \$0.4 million and \$28.6 million for the years ended September 30, 2022 and 2021, respectively. The effective tax rates used to calculate our income tax benefit for the years ended September 30, 2022 and 2021 were 0.4% and 26.6%, respectively. We recorded an income tax benefit in 2022 due to the release of a state tax reserve during the year. We recorded an income tax benefit in 2021 due to a federal net operating loss carryback available under the CARES Act for our fiscal year 2021, which is no longer available after September 30, 2021.

As of September 30, 2022 and 2021, we continue to record a valuation allowance against our deferred tax assets because it is more likely than not that we will not have sufficient taxable income in the future that would allow us to realize the majority of our deferred tax assets.

#### **Comparison of the Years Ended September 30, 2021 and 2020**

For a discussion of our results of operations for the year ended September 30, 2021, as compared to the year ended September 30, 2020, see Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—Results of Operations—Comparison of the Years Ended September 30, 2021 and 2020 included in our Annual Report on Form 10-K for the fiscal year ended September 30, 2021.

#### **Liquidity and Capital Resources**

We fund our operations with cash flows from our royalty revenue and our existing financial resources. At September 30, 2022, our principal sources of liquidity were cash and cash equivalents and short-term and long-term marketable securities of \$278.5 million.

The following table shows a summary of our cash flows:

	Years Ended September 30,		
	2022	2021	2020
	(in thousands)		
Cash provided by (used in):			
Operating activities	\$ (84,782)	\$ (69,996)	\$ 7,088
Investing activities	54,897	36,991	19,830
Financing activities	20,033	3,080	8,983
Net increase (decrease) in cash, cash equivalents and restricted cash	\$ (9,852)	\$ (29,925)	\$ 35,901

#### **Net cash used in operating activities**

Cash used in operating activities was \$84.8 million for the year ended September 30, 2022 as compared to cash used in operating activities of \$70.0 million for the same period in 2021. The increase in cash used in operating activities was primarily driven by a decrease in royalty payments received under our collaboration with AbbVie.

#### **Net cash provided by investing activities**

The increase of \$17.9 million in cash provided by investing activities for the year ended September 30, 2022, as compared to the same period in 2021, was driven primarily by the timing of purchases, sales and maturities of marketable securities.

#### **Net cash provided by financing activities**

The increase in cash provided by financing activities of \$17.0 million for the year ended September 30, 2022, as compared to 2021, was driven by an increase in proceeds from stock option exercises.

### ***Year Ended September 30, 2021***

For a discussion of our cash flows for the year ended September 30, 2021, see Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and Capital Resources—Cash Flows included in our Annual Report on Form 10-K for the fiscal year ended September 30, 2021.

### ***Funding Requirements***

As of September 30, 2022, we had \$278.5 million in cash, cash equivalents and short-term and long-term marketable securities. We believe that our existing cash, cash equivalents and short-term and long-term marketable securities as of September 30, 2022, and cash flows from our continuing HCV royalties will be sufficient to meet our anticipated cash requirements into approximately the fourth quarter of fiscal 2024. However, our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially.

Our future capital requirements are difficult to forecast and will depend on many factors, including:

- the amount of royalties generated from MAVYRET/MAVIRET sales under our existing collaboration with AbbVie;
- any continuing impact of the COVID-19 pandemic on the number of treated HCV patients;
- the number and characteristics of our research and development programs;
- the scope, progress, results and costs of researching and developing our product candidates on our own, including conducting advanced clinical trials;
- delays and additional expense in our clinical trials as a result of COVID-19;
- the cost of manufacturing our product candidates for clinical development and any products we successfully commercialize independently;
- our ability to establish new collaborations, licensing or other arrangements, if any, and the financial terms of such arrangements;
- opportunities to in-license or otherwise acquire new technologies and therapeutic candidates;
- the timing of, and the costs involved in, obtaining regulatory approvals for any product candidates we develop independently;
- the cost of commercialization activities, if any, of any product candidates we develop independently that are approved for sale, including marketing, sales and distribution costs;
- the timing and amount of any sales of our product candidates, if any, or royalties thereon;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patents, including any litigation costs and the outcomes of any such litigation; and
- potential fluctuations in foreign currency exchange rates.

### **Off-Balance Sheet Arrangements**

We do not engage in any off-balance sheet financing activities. We do not have any interest in entities referred to as variable interest entities or unconsolidated entities, which include special purpose entities and other structured finance entities.

### **Recently Issued Accounting Pronouncements**

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is set forth in Note 2 to the consolidated financial statements included in this Annual Report on Form 10-K.

### **Contractual Obligations and Commitments**

We currently lease space in Watertown, Massachusetts, under two separate lease agreements with one landlord. We have entered into a third lease agreement with the same landlord to lease additional laboratory and office space at a to-be-constructed facility located at Arsenal on the Charles in Watertown, Massachusetts.

Our first lease for office and laboratory space at 500 Arsenal Street expires on September 1, 2027. In May 2022, we entered into a new ten-year lease for laboratory and office space in Watertown, Massachusetts, adjacent to our 400 Talcott Avenue premises at Arsenal on the Charles, at a to-be-constructed facility. We currently anticipate we will gain access to construct tenant improvements in October 2023. In connection with this lease, we amended our 500 Arsenal Street lease to shorten the expiration date from September 1, 2027, to the date the Arsenal on the Charles facility is ready for our occupancy.

The second lease for office space located at 400 Talcott Avenue, commenced on September 24, 2018 for a term of six years. In May 2022, we amended this lease to expand the rented space and extend the lease term through June 1, 2034. We expect to spend approximately \$7.6 million in capital expenditures for the additional space, which primarily relate to tenant improvements. We are eligible to receive a tenant improvement allowance from the landlord of up to \$2.6 million.

As of September 30, 2022, we had 1.9 million outstanding shares of Series 1 nonconvertible preferred stock, all of which we classified as a long-term liability on our consolidated balance sheet and recorded at fair value of \$1.4 million. The fair value of the preferred stock was measured based on significant inputs not observable in the market, which represented a Level 3 measurement within the fair value hierarchy. The fair value of these instruments represents less than 10% of liabilities as of September 30, 2022. The Series 1 nonconvertible preferred stock issued would require the payment of \$2.0 million in the event of a qualifying merger or sale of the company.

## **ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK**

### ***Interest Rate Risk***

We had cash, cash equivalents and short-term and long-term marketable securities of \$278.5 million and \$352.4 million at September 30, 2022 and 2021, respectively, which consisted of cash, money market funds, corporate bonds, commercial paper and treasury notes. Interest income is sensitive to changes in the general level of interest rates; however, due to the nature of these investments, a change in market interest rates of 1% would not be expected to have a material impact on our financial condition or results of operations for either period. We had no debt outstanding as of September 30, 2022 or 2021.

### ***Foreign Exchange Risk***

As we continue to progress our wholly-owned programs into clinical development, we will conduct clinical trials and clinical manufacturing outside of the U.S. and thus will face exposure to movements in foreign currency exchange rates, primarily the British Pound and Euro, against the U.S. Dollar, arising from our accounts payable and accrued expenses. During fiscal 2022 and 2021, the impact of foreign currency exposure was immaterial and thus did not have a significant impact on our consolidated financial statements. Our operations may become subject to more significant fluctuations in foreign currency exchange rates in the future if we continue to contract with vendors outside of the U.S.

## **ITEM 8. CONSOLIDATED FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

Our consolidated financial statements, together with the report of our independent registered public accounting firm, appear on pages F-1 through F-25 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**

### **Disclosure Controls and Procedures and Internal Control over Financial Reporting**

#### ***Evaluation of Disclosure Controls and Procedures***

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the Company's reports under the Securities Exchange Act of 1934, as amended, or the Exchange Act, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to management, including our Chief Executive Officer (CEO) and Chief Financial Officer (CFO), as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, as the Companies are designed to do, and management necessarily was required to apply its judgment in evaluating the risk related to controls and procedures.

In connection with the preparation of this Form 10-K, as of September 30, 2022, an evaluation was performed under the supervision and with the participation of our management, including the CEO and CFO, of the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). Based on that evaluation, our CEO and CFO concluded that our disclosure controls and procedures were effective at a reasonable assurance level as of September 30, 2022. These conclusions were communicated to the Audit Committee.

#### *Changes in Internal Control over Financial Reporting*

There were no changes in our internal control over financial reporting that occurred during the quarter ended September 30, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

#### *Management's Report on Internal Control over Financial Reporting*

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rule 13a-15(f) and Rule 15d-15(f) under the Exchange Act. Our internal control system is designed to provide reasonable assurance to the Company's management and Board of Directors regarding the preparation and fair presentation of published financial statements. All internal control systems, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation.

Our management has assessed the effectiveness of our internal control over financial reporting as of September 30, 2022. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in its 2013 *Internal Control—Integrated Framework*. Based on this assessment, our management has concluded that as of September 30, 2022, our internal control over financial reporting is effective.

The effectiveness of the Company's internal control over financial reporting as of September 30, 2022, has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their attestation report, which appears in Item 8 above.

#### **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

Portions of the response to this item are incorporated herein by reference from the discussion responsive thereto in the Company's Definitive Proxy Statement relating to the 2023 Annual Meeting of Stockholders, also referred to as the 2023 Proxy Statement, which will be filed within 120 days after September 30, 2022.

We have adopted a Code of Business Conduct and Ethics (the code of ethics) that applies to all of our employees, officers and directors. The code of ethics is available on our website at <http://www.enanta.com>. In addition, if we make any substantive amendments to the code of ethics or grant any waiver, including any implicit waiver, from a provision of the code to any of our executive officers or directors, we will disclose the nature of such amendment or waiver as required by applicable law on our website or on a Form 8-K.

### ITEM 11. EXECUTIVE COMPENSATION

The response to this item is incorporated herein by reference from the discussion responsive thereto in the 2023 Proxy Statement, which will be filed within 120 days after September 30, 2022.

### ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The response to this item is incorporated herein by reference in part from the discussion responsive thereto in the 2023 Proxy Statement, which will be filed within 120 days after September 30, 2022.

The following table provides information about the securities authorized for issuance under the Company's equity compensation plans as of September 30, 2022:

**Equity Compensation Plan Information**  
(in thousands, except per share information)

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)	Weighted average exercise price of outstanding options, warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c)
Equity compensation plans approved by security holders <sup>(1)</sup>	4,414 <sup>(2)</sup>	\$ 48.46	1,549 <sup>(3)</sup>
Equity compensation plans not approved by security holders	—	—	—
<b>Totals</b>	<b>4,414</b>		<b>1,549</b>

<sup>(1)</sup> Consists of the Company's 2019 Equity Incentive Plan, the Company's 2012 Equity Incentive Plan, as amended, the Company's Amended and Restated 1995 Equity Incentive Plan, as amended, and the Company's Employee Stock Purchase Plan.

<sup>(2)</sup> Consists of shares of the Company's common stock issuable upon exercise of outstanding options issued under the Company's 2019 Equity Incentive Plan, the Company's Amended and Restated 2012 Equity Incentive Plan and the Company's Amended and Restated 1995 Equity Incentive Plan.

<sup>(3)</sup> Consists of shares of the Company's common stock reserved for future issuance under the Company's 2019 Equity Incentive Plan and the Company's Employee Stock Purchase Plan.

**ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE**

The response to this item is incorporated herein by reference from the discussion responsive thereto in the 2023 Proxy Statement, which will be filed within 120 days after September 30, 2022.

**ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES**

The response to this item is incorporated herein by reference from the discussion responsive thereto in the 2023 Proxy Statement, which will be filed within 120 days after September 30, 2022.

## PART IV

### ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

#### (a) 1. FINANCIAL STATEMENTS

The financial statements are included under Part II, Item 8 of this Report.

#### 2. FINANCIAL STATEMENTS SCHEDULE

Schedules are omitted because they are not applicable, or are not required, or because the information is included in the consolidated financial statements and notes thereto.

#### 3. EXHIBITS –

The exhibits are listed below under Part IV, Item 15(b) of this Report.

#### (b) EXHIBITS

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed Herewith
		Form	Date	Exhibit Number	File Number	
3.1	Restated Certificate of Incorporation of Enanta Pharmaceuticals, Inc.	8-K	03/28/2013	3.1	001-35839	
3.2	Amended and Restated Bylaws of Enanta Pharmaceuticals, Inc. (as amended and restated in August 2015).	8-K	08/18/2015	3.2	001-35839	
4.1	Specimen certificate evidencing shares of common stock.	S-1/A	02/05/2013	4.1	333-184779	
4.2	Specimen certificate evidencing shares of Series 1 Non-Convertible Preferred Stock	10-K	12/11/2017	4.3	001-35839	
4.3	Description of securities registered pursuant to Section 12 of the Securities Exchange Act of 1934	10-K	11/27/2019	4.3	001-35839	
10.1#	Form of Indemnification Agreement for directors and officers.	S-1/A	02/05/2013	10.7	333-184779	
10.2#	Amended and Restated Employment Agreement between the Company and Jay R. Luly, Ph.D., dated as of March 4, 2013.	S-1/A	03/05/2013	10.5	333-184779	
10.3#	Form of Amended and Restated Employment Agreement for Executive Officers other than the Chief Executive Officer.	S-1/A	03/05/2013	10.17	333-184779	
10.4†	Collaborative Development and License Agreement between the Company and Abbott Laboratories, dated November 27, 2006; as amended by a First Amendment to Collaborative Development and License Agreement dated January 27, 2009 and a Second Amendment to Collaborative Development and License Agreement dated December 9, 2009 (assigned to AbbVie Inc. as of January 1, 2013).	8-K	02/05/2021	10.1	001-35839	
10.5†	Third Amendment to Collaborative Development and License Agreement between the Company and AbbVie dated October 20, 2014.	8-K	02/05/2021	10.2	001-35839	
10.6	Fourth Amendment to Collaborative Development and License Agreement between the Company and AbbVie dated as of March 3, 2015.	10-Q	05/08/2015	10.1	001-35839	
10.7	Lease Agreement between Company and ARE-500 Arsenal Street LLC, dated as of April 15, 2011.	S-1	11/06/2012	10.6	333-184779	
10.8	First Amendment to Lease Agreement made as of March 5, 2015 between the Company and ARE-500 Arsenal Street LLC.	10-Q	05/08/2015	10.2	001-35839	

10.9	<a href="#">Second Amendment to Lease made as of May 12, 2022 by and between ARE-500 Arsenal Street, LLC and the Company.</a>	8-K	05/17/2022	10.1	001-35839
10.10	Lease Agreement between Company and Athena Arsenal, LLC, dated as of September 27, 2018.	10-K	11/29/2018	10.10	001-35839
10.11	<a href="#">First Amendment to Lease Agreement made as of May 12, 2022 by and between ARE-MA Region No. 75, LLC and the Company.</a>	8-K	05/17/2022	10.2	001-35839
10.12	<a href="#">Lease Agreement made as of May 12, 2022 by and between ARE-MA Region No. 75, LLC and the Company.</a>	8-K	05/17/2022	10.3	001-35839
10.13#	Amended and Restated 1995 Equity Incentive Plan.	S-1/A	03/05/2013	10.8	333-184779
10.14#	Form of Incentive Stock Option Certificate under Amended and Restated 1995 Equity Incentive Plan.	S-1/A	03/05/2013	10.9	333-184779
10.15#	Form of Non-Statutory Stock Option Certificate under Amended and Restated 1995 Equity Incentive Plan.	S-1/A	03/05/2013	10.10	333-184779
10.16#	Form of Non-Statutory Stock Option Certificate for directors under Amended and Restated 1995 Equity Incentive Plan.	S-1/A	03/05/2013	10.11	333-184779
10.17#	2012 Equity Incentive Plan (As adjusted to reflect the application of the 1-for-4.31 reverse stock split of the Company's common stock effected on March 1, 2013).	10-K/A	01/06/2017	10.14	001-35839
10.17#	Form of Incentive Stock Option Agreement under 2012 Equity Incentive Plan.	S-1/A	03/05/2013	10.13	333-184779
10.18#	Form of Non-Statutory Stock Option Agreement under 2012 Equity Incentive Plan.	S-1/A	03/05/2013	10.14	333-184779
10.19#	Form of Non-Statutory Stock Option Certificate for directors under 2012 Equity Incentive Plan.	S-1/A	03/05/2013	10.15	333-184779
10.20#	Form of Performance Share Unit Certificate under 2012 Equity Incentive Plan.	10-K	12/11/2017	10.18	001-35839
10.21#	Form of Relative Total Stockholder Return Unit Certificate under 2012 Equity Incentive Plan.	10-K	12/11/2017	10.19	001-35839
10.22#	Employee Stock Purchase Plan.	S-1/A	02/05/2013	10.16	333-184779
10.23#	<a href="#">2019 Equity Incentive Plan (As amended March 2022)</a>	8-K	03/08/2022	10.1	001-35839
10.24#	Form of Notice of Grant of Non-Statutory Stock Option under 2019 Equity Incentive Plan.	10-Q	05/10/2019	10.2	001-35839
10.25#	Form of Notice of Grant of Non-Statutory Stock Option for Directors under 2019 Equity Incentive Plan.	10-Q	05/10/2019	10.3	001-35839
10.26#	Form of Relative Total Stockholder Return Unit Certificate under 2019 Equity Incentive Plan.	10-Q	05/10/2019	10.4	001-35839
10.27#	Form of Performance Share Unit Certificate under 2019 Equity Incentive Plan.	10-Q	05/10/2019	10.5	001-35839
10.28#	Form of Notice of Restricted Stock Unit Award under 2019 Equity Incentive Plan.	10-K	11/25/2020	10.27	001-35839
21.1	Subsidiaries of the Company.				X
23.1	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm.				X



31.1	Certification of the Chief Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.	X
31.2	Certification of Chief Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.	X
32.1	Certification of the Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.	X
101.SCH	Inline XBRL Taxonomy Extension Schema Document	
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)	

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# Management contract or compensatory plan, contract or agreement.

† Confidential treatment granted as to portions of this Exhibit. The confidential portions of this Exhibit have been omitted and are marked by asterisks.

†† This Exhibit has been filed separately with the commission pursuant to an application for confidentiality treatment. The confidential portions of this Exhibit have been omitted and are marked by asterisks.

#### **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 Company has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, this 23th day of November, 2022.

**ENANTA PHARMACEUTICALS, INC.**

By: /s/ Jay R. Luly, Ph.D.  
Jay R. Luly, Ph.D.  
*Chief Executive Officer*

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

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Jay R. Luly, Ph.D.</u> Jay R. Luly, Ph.D.	President and Chief Executive Officer and Director (Principal Executive Officer)	November 23, 2022
<u>/s/ Paul J. Mellett</u> Paul J. Mellett	Chief Financial Officer (Principal Financial and Accounting Officer)	November 23, 2022
<u>/s/ Bruce L.A. Carter, Ph.D.</u> Bruce L.A. Carter, Ph.D.	Director	November 23, 2022
<u>/s/ Mark G. Foletta</u> Mark G. Foletta	Director	November 23, 2022
<u>/s/ Yujiro S. Hata</u> Yujiro S. Hata	Director	November 23, 2022
<u>/s/ Kristine Peterson</u> Kristine Peterson	Director	November 23, 2022
<u>/s/ Lesley Russell, MB. Ch.B., MRCP</u> Lesley Russell, MB. Ch.B., MRCP	Director	November 23, 2022
<u>/s/ Terry Vance</u> Terry Vance	Director	November 23, 2022

**ITEM 8. CONSOLIDATED FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

**ENANTA PHARMACEUTICALS, INC.**

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## **Report of Independent Registered Public Accounting Firm**

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

### ***Opinions on the Financial Statements and Internal Control over Financial Reporting***

We have audited the accompanying consolidated balance sheets of Enanta Pharmaceuticals, Inc. and its subsidiary (the “Company”) as of September 30, 2022 and 2021, and the related consolidated statements of operations, of comprehensive loss, of stockholders’ equity and of cash flows for each of the three years in the period ended September 30, 2022, including the related notes (collectively referred to as the “consolidated financial statements”). We also have audited the Company's internal control over financial reporting as of September 30, 2022, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of September 30, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended September 30, 2022 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of September 30, 2022, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO.

### ***Basis for Opinions***

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management’s Report on Internal Control over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company’s consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements 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. 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 audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

### ***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 (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) 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 (iii) 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.



## ***Critical Audit Matters***

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

### ***Research and Development and Pharmaceutical Drug Manufacturing Accruals***

As described in Notes 2 and 6 to the consolidated financial statements, the Company has entered into various contracts with third parties to perform research and development and pharmaceutical drug manufacturing. When billing terms under these contracts do not coincide with the timing of when the work is performed, management is required to make estimates of outstanding obligations to those third parties as of period end. Within accrued expenses and other current liabilities, total accrued research and development expenses and accrued pharmaceutical drug manufacturing amounted to \$5.5 million and \$6.9 million as of September 30, 2022, respectively. The accrual estimates are based on a number of factors, including management's knowledge of the research and development programs and pharmaceutical drug manufacturing activities and associated timelines, invoicing to date, and the provisions in the contract. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period.

The principal considerations for our determination that performing procedures relating to research and development and pharmaceutical drug manufacturing accruals is a critical audit matter are the significant judgment by management in developing the accrual estimates, as the estimates are based on a number of factors, including management's knowledge of the research and development programs and pharmaceutical drug manufacturing activities and associated timelines, invoicing to date, and the provisions in the contracts, which in turn led to a high degree of auditor judgment, subjectivity and effort in performing procedures and evaluating management's significant assumptions related to progress towards completion of the research and development programs and pharmaceutical drug manufacturing activities.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included testing the effectiveness of controls relating to accrued research and development expenses and accrued pharmaceutical drug manufacturing, including controls over the review of contracts and assessment of progress of the accrued research and development programs and accrued pharmaceutical drug manufacturing activities. These procedures also included, among others (i) testing management's process for developing estimates based upon the progress of the research and development programs and pharmaceutical drug manufacturing activities; (ii) evaluating the appropriateness of the method used by management to develop the estimates; (iii) reading research and development and pharmaceutical drug manufacturing contracts on a test basis; (iv) evaluating the completeness and accuracy of data used by management; and (v) evaluating the reasonableness of significant assumptions related to the progress towards completion. Evaluating management's assumptions related to progress towards completion of the research and development programs and pharmaceutical drug manufacturing activities included evaluating whether the assumptions were reasonable considering the associated timelines, invoicing to date and the provisions in the contracts.

/s/ PricewaterhouseCoopers LLP  
Boston, Massachusetts  
November 23, 2022

We have served as the Company's auditor since 1999.

**ENANTA PHARMACEUTICALS, INC.**

**CONSOLIDATED BALANCE SHEETS**  
(in thousands, except per share data)

	September 30, 2022	September 30, 2021
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 43,994	\$ 57,206
Short-term marketable securities	205,238	186,796
Accounts receivable	20,318	23,576
Prepaid expenses and other current assets	13,445	14,188
Income tax receivable	28,718	37,255
Total current assets	311,713	319,021
Long-term marketable securities	29,285	108,416
Property and equipment, net	6,173	5,943
Operating lease, right-of-use assets	23,575	4,711
Restricted cash	3,968	608
Other long-term assets	696	92
Total assets	<u>\$ 375,410</u>	<u>\$ 438,791</u>
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 6,000	\$ 9,540
Accrued expenses and other current liabilities	20,936	22,429
Operating lease liabilities	2,891	4,203
Total current liabilities	29,827	36,172
Operating lease liabilities, net of current portion	22,372	1,126
Series 1 nonconvertible preferred stock	1,423	1,506
Other long-term liabilities	454	558
Total liabilities	54,076	39,362
Commitments and contingencies (Note 12)		
Stockholders' equity:		
Common stock; \$0.01 par value per share, 100,000 shares authorized; 20,791 and 20,238 shares issued and outstanding at September 30, 2022 and September 30, 2021, respectively	208	202
Additional paid-in capital	398,029	351,033
Accumulated other comprehensive loss	(3,724)	(382)
Retained earnings (accumulated deficit)	(73,179)	48,576
Total stockholders' equity	321,334	399,429
Total liabilities and stockholders' equity	<u>\$ 375,410</u>	<u>\$ 438,791</u>

The accompanying notes are an integral part of these consolidated financial statements.

**ENANTA PHARMACEUTICALS, INC.**  
**CONSOLIDATED STATEMENTS OF OPERATIONS**  
(in thousands, except per share data)

	Years Ended September 30,		
	2022	2021	2020
Royalty revenue	\$ 86,160	\$ 97,074	\$ 122,473
Operating expenses:			
Research and development	164,522	174,111	136,756
General and administrative	45,482	32,536	27,356
Total operating expenses	210,004	206,647	164,112
Loss from operations	(123,844)	(109,573)	(41,639)
Other income (expense):			
Interest and investment income, net	1,573	2,021	6,471
Change in fair value of Series 1 nonconvertible preferred stock	83	(27)	149
Total other income, net	1,656	1,994	6,620
Loss before income taxes	(122,188)	(107,579)	(35,019)
Income tax benefit (expense)	433	28,583	(1,149)
Net loss	\$ (121,755)	\$ (78,996)	\$ (36,168)
Net loss per share, basic and diluted	\$ (5.91)	\$ (3.92)	\$ (1.81)
Weighted average common shares outstanding, basic and diluted	20,603	20,171	19,940

The accompanying notes are an integral part of these consolidated financial statements.

**ENANTA PHARMACEUTICALS, INC.**  
**CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS**  
**(in thousands)**

	<b>Years Ended September 30,</b>		
	<b>2022</b>	<b>2021</b>	<b>2020</b>
Net loss	\$ (121,755)	\$ (78,996)	\$ (36,168)
Other comprehensive income (loss):			
Net unrealized gains (losses) on marketable securities, net of tax expense of \$0, \$0, and \$388	(3,342)	(1,226)	698
Total other comprehensive income (loss), net of tax	(3,342)	(1,226)	698
Comprehensive loss	<u>\$ (125,097)</u>	<u>\$ (80,222)</u>	<u>\$ (35,470)</u>

The accompanying notes are an integral part of these consolidated financial statements.



**ENANTA PHARMACEUTICALS, INC.**

**CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY**  
(in thousands)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Retained Earnings (Accumulated Deficit)	Total Stockholders' Equity
	Shares	Amount				
<b>Balances at September 30, 2019</b>	19,703	\$	197	\$	146	\$
Exercise of stock options	327		4	10,477	—	10,481
Vesting of restricted stock units, net of withholding	47		—	(1,498)	—	(1,498)
Stock-based compensation expense	—		—	19,575	—	19,575
Other comprehensive income, net of tax	—		—	—	698	698
Net loss	—		—	—	(36,168)	(36,168)
<b>Balances at September 30, 2020</b>	20,077		201	326,963	844	127,572
Exercise of stock options	129		1	3,613	—	3,614
Vesting of restricted stock units, net of withholding	32		—	(534)	—	(534)
Stock-based compensation expense	—		—	20,991	—	20,991
Other comprehensive loss	—		—	—	(1,226)	(1,226)
Net loss	—		—	—	(78,996)	(78,996)
<b>Balances at September 30, 2021</b>	20,238		202	351,033	(382)	48,576
Exercise of stock options	517		6	21,256	—	21,262
Vesting of restricted stock units, net of withholding	36		—	(1,229)	—	(1,229)
Stock-based compensation expense	—		—	26,969	—	26,969
Other comprehensive loss	—		—	—	(3,342)	(3,342)
Net loss	—		—	—	(121,755)	(121,755)
<b>Balances at September 30, 2022</b>	20,791	\$	208	\$	398,029	\$
					(3,724)	(73,179)
						\$
						321,334

The accompanying notes are an integral part of these consolidated financial statements.

**ENANTA PHARMACEUTICALS, INC.**  
**CONSOLIDATED STATEMENTS OF CASH FLOWS**  
(in thousands)

	Years Ended September 30,		
	2022	2021	2020
<b>Cash flows from operating activities</b>			
Net loss	\$ (121,755)	\$ (78,996)	\$ (36,168)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:			
Stock-based compensation expense	26,969	20,991	19,575
Depreciation and amortization expense	2,973	3,334	3,644
Deferred income taxes	—	345	10,608
Premium paid on marketable securities	(846)	(4,028)	(3,575)
Amortization of premium on marketable securities	1,171	2,116	304
Change in fair value of Series 1 nonconvertible preferred stock	(83)	27	(149)
Other non-cash items	—	(97)	(51)
Change in operating assets and liabilities:			
Accounts receivable	3,258	(84)	27,821
Prepaid expenses and other current assets	743	(533)	(7,270)
Income tax receivable	8,537	(24,214)	(4,127)
Operating lease, right-of-use assets	4,776	5,418	3,184
Other long-term assets	(604)	—	—
Accounts payable	(4,634)	3,774	(883)
Accrued expenses	(1,477)	8,350	(1,368)
Operating lease liabilities	(3,706)	(5,879)	(3,535)
Other long-term liabilities	(104)	(520)	(922)
Net cash provided by (used in) operating activities	(84,782)	(69,996)	7,088
<b>Cash flows from investing activities</b>			
Purchase of marketable securities	(171,446)	(307,348)	(338,553)
Proceeds from maturities and sale of marketable securities	228,468	345,089	359,828
Purchase of property and equipment	(2,125)	(750)	(1,445)
Net cash provided by investing activities	54,897	36,991	19,830
<b>Cash flows from financing activities</b>			
Proceeds from exercise of stock options	21,262	3,614	10,481
Payments for settlement of share-based awards	(1,229)	(534)	(1,498)
Net cash provided by financing activities	20,033	3,080	8,983
<b>Net increase (decrease) in cash, cash equivalents and restricted cash</b>	<b>(9,852)</b>	<b>(29,925)</b>	<b>35,901</b>
Cash, cash equivalents and restricted cash at beginning of period	57,814	87,739	51,838
Cash, cash equivalents and restricted cash at end of period	<u>\$ 47,962</u>	<u>\$ 57,814</u>	<u>\$ 87,739</u>
<b>Supplemental cash flow information:</b>			
Cash paid for taxes	\$ —	\$ 32	\$ 105
<b>Supplemental disclosure of noncash information:</b>			
Purchases of fixed assets included in accounts payable and accrued expenses	\$ 1,215	\$ 137	\$ 188
Operating lease liabilities arising from obtaining right-of-use assets	\$ 23,910	\$ 3,320	\$ 3,053

The accompanying notes are an integral part of these consolidated financial statements.

**ENANTA PHARMACEUTICALS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**  
**(Amounts in thousands, except per share data)**

**1. Nature of the Business**

Enanta Pharmaceuticals, Inc. (the “Company”), incorporated in Delaware in 1995, is a biotechnology company that uses its robust, chemistry-driven approach and drug discovery capabilities to become a leader in the discovery and development of small molecule drugs, with an emphasis on treatments for viral infections. The Company discovered glecaprevir, the second of two protease inhibitors discovered and developed through its collaboration with AbbVie for the treatment of chronic infection with hepatitis C virus (“HCV”). Glecaprevir is co-formulated as part of AbbVie’s leading direct-acting antiviral (“DAA”) combination treatment for HCV, which is marketed under the tradenames MAVYRET® (U.S.) and MAVIRET® (ex-U.S.) (glecaprevir/pibrentasvir). Royalties from the Company’s AbbVie collaboration and its existing financial resources provide funding to support the Company’s wholly-owned research and development programs, which are primarily focused on the following disease targets: respiratory syncytial virus (“RSV”), SARS-CoV-2, hepatitis B virus (“HBV”) and human metapneumovirus (“hMPV”).

The Company is subject to many of the risks common to companies in the biotechnology industry, including but not limited to, the uncertainties of research and development, competition from technological innovations of others, dependence on collaborative arrangements, protection of proprietary technology, dependence on key personnel and compliance with government regulation. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approvals, prior to commercialization. These efforts require significant amounts of capital, adequate personnel and infrastructure, and extensive compliance reporting capabilities.

**COVID-19**

In March 2020, the World Health Organization declared COVID-19 a global pandemic and countries worldwide implemented various measures to contain the spread of the SARS-CoV-2 virus. National, state and local governments in affected regions have implemented and may continue to implement varying safety precautions, including quarantines, border closures, increased border controls, travel restrictions, shelter-in-place orders and shutdowns, business closures, cancellations of public gatherings and other measures. The extent and severity of the impact on the Company’s business and clinical trials will be determined largely by the extent to which there are disruptions in the supply chains for its research and product candidates, delays in the conduct of ongoing and future clinical trials, or reductions in the number of patients accessing AbbVie’s HCV regimens, or any combination of those events. In addition, AbbVie experienced a decline in HCV sales compared to periods prior to March 2020 as a result of a reduction in patients accessing AbbVie’s HCV regimens due to the COVID-19 pandemic.

The full extent to which the COVID-19 pandemic will directly or indirectly impact the Company’s business, results of operations and financial condition will depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning COVID-19 and its variants and public health actions taken to contain it, as well as the cumulative economic impact of both of those factors.

**2. Summary of Significant Accounting Policies**

**Basis of Presentation**

The accompanying consolidated financial statements include those of the Company and its subsidiary, Enanta Pharmaceuticals Security Corporation, after elimination of all intercompany accounts and transactions. The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (“GAAP”). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification and Accounting Standards Update (“ASU”) of the Financial Accounting Standards Board (“FASB”).

**Use of Estimates**

The preparation of consolidated financial statements in conformity with GAAP requires management 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 consolidated financial statements, and the reported amounts of revenues and expenses during the reporting period. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, management’s judgments with respect to its revenue arrangements; valuation of stock-based awards and the accrual of research and development expenses. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. The future developments of the COVID-19 pandemic also may directly or indirectly impact the Company’s business. The Company has made estimates of the impact of COVID-19 in the Company’s consolidated financial statements as of September 30, 2022. Actual results could differ from the Company’s estimates.

## **Cash Equivalents and Marketable Securities**

The Company considers all short-term, highly liquid investments with original maturities of ninety days or less at acquisition date to be cash equivalents. Marketable securities with original maturities of greater than ninety days and remaining maturities of less than one year from the balance sheet date are classified as short-term marketable securities. Marketable securities with remaining maturities of greater than one year from the balance sheet date are classified as long-term marketable securities.

The Company classifies all of its marketable securities as available-for-sale. The Company continually evaluates the credit ratings of its investment portfolio and underlying securities. The Company invests in accordance with its investment policy and invests at the date of purchase in securities with a rating of A3/A- or higher according to Moody's or S&P or A- by Fitch. The Company reports available-for-sale investments at fair value as of each balance sheet date and records any unrealized gains or losses as a component of stockholders' equity. The cost of securities sold is determined on a specific identification basis and realized gains and losses are included in other income (expense) within the consolidated statements of operations. When the fair value is below the amortized cost of a marketable security, an estimate of expected credit losses is made. The credit-related impairment amount is recognized in the consolidated statements of operations. Credit losses are recognized through the use of an allowance for credit losses account in the consolidated balance sheet and subsequent improvements in expected credit losses are recognized as a reversal of an amount in the allowance account. If the Company has the intent to sell the security or it is more likely than not that the Company will be required to sell the security prior to recovery of its amortized cost basis, then the allowance for the credit loss is written-off and the excess of the amortized cost basis of the asset over its fair value is recorded in the consolidated statements of operations. There were no credit losses recorded during the years ended September 30, 2022, 2021, and 2020.

## **Restricted Cash**

As of September 30, 2022 and 2021 the Company had outstanding letters of credit collateralized by a money market account of \$3,968 and \$608, respectively, to the benefit of the landlord of the Company's building leases. These amounts were classified as long-term restricted cash as of September 30, 2022 and 2021.

## **Concentration of Credit Risk and of Significant Customers and Suppliers**

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents, short-term and long-term marketable securities and accounts receivable. The Company has all cash and investment balances at one accredited financial institution, including cash in amounts that exceed federally insured limits. The Company does not believe it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company has historically generated the majority of its revenue from its collaborative research and license agreements. As of September 30, 2022 and 2021, accounts receivable consisted of amounts due from the Company's principal collaborator (see Note 7).

The Company is completely dependent on third-party manufacturers for product supply for preclinical and clinical research activities. The Company relies and expects to continue to rely exclusively on several manufacturers to supply the Company with its drug supply requirements related to these activities. These research programs would be adversely affected by a significant interruption in the supply from these third-party manufacturers.

## **Fair Value Measurements**

Certain assets and liabilities are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. A fair value hierarchy is based on three levels of inputs that are used to measure fair value, of which the first two levels are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices) such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.



The Company's instruments that are carried at fair value are cash equivalents, short-term and long-term marketable securities and the Series 1 nonconvertible preferred stock. The carrying values of accounts receivable, prepaid and other assets, accounts payable and accrued expenses approximate their fair value due to the short-term nature of these assets and liabilities.

### Property and Equipment

Property and equipment are stated at cost less accumulated depreciation. Depreciation expense is recognized using the straight-line method over the following estimated useful lives:

Laboratory and office equipment	5 years
Leasehold improvements	Shorter of life of lease or estimated useful life
Purchased software	3 years
Computer equipment	3 years
Furniture	7 years

Expenditures for repairs and maintenance of assets are charged to expense as incurred. Costs of major additions and betterments are capitalized and depreciated on a straight-line basis over their useful lives. Upon retirement or sale, the cost and related accumulated depreciation of assets disposed are removed from the accounts and any resulting gain or loss is included in income from operations in the consolidated statements of operations.

### Leases

The Company accounts for a contract as a lease when it has the right to control the asset for a period of time while obtaining substantially all of the asset's economic benefits. The Company determines if an arrangement is a lease or contains an embedded lease at inception. For arrangements that meet the definition of a lease, the Company determines the initial classification and measurement of its right-of-use asset and lease liability at the lease commencement date and thereafter if modified. The lease term includes any renewal options that the Company is reasonably assured to exercise. The present value of lease payments is determined by using the interest rate implicit in the lease, if that rate is readily determinable; otherwise, the Company uses its estimated secured incremental borrowing rate for that lease term. The Company's policy is to not record leases with an original term of 12 months or less on its consolidated balance sheets and recognizes those lease payments in the consolidated statements of operations on a straight-line basis over the lease term.

In addition to rent, the leases may require the Company to pay additional costs, such as utilities, maintenance and other operating costs, which are generally referred to as non-lease components. The Company has elected to not separate lease and non-lease components. Only the fixed costs for lease components and their associated non-lease components are accounted for as a single lease component and recognized as part of a right-of-use asset and lease liability. Rent expense for operating leases is recognized on a straight-line basis over the reasonably assured lease term based on the total lease payments and is included in operating expense in the consolidated statements of operations.

### Impairment of Long-Lived Assets

The Company reviews long-lived assets, primarily property and equipment and right-of-use assets, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends, and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset over its fair value, determined based on discounted cash flows. To date, the Company has not recorded any impairment losses on long-lived assets.

### Revenue Recognition

The Company's revenue has been generated primarily through collaborative research and license agreements. The terms of these agreements contain multiple deliverables, which may include (i) licenses, (ii) research and development activities, and (iii) participation in joint research and development steering committees. The terms of these agreements may include nonrefundable upfront license fees, payments for research and development activities, payments based upon the achievement of certain milestones, and royalty payments based on product sales derived from the collaboration.

The Company recognizes revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the Company expects to be entitled in exchange for those goods or services. The Company receives sales-based

royalties for which the license is deemed to be the predominant item to which the royalties relate and thus the Company recognizes sales-based royalties as the underlying sales are earned.

### **Research and Development Costs**

Included in research and development costs are wages, stock-based compensation and benefits of employees performing research and development, third-party license fees and other operational costs related to the Company's research and development activities, including facility-related expenses and external costs of outside contractors engaged to conduct both preclinical and clinical studies and manufacture quantities of product for preclinical and clinical studies. The Company expenses the cost of each contract as the work is performed.

Upfront payments and milestone payments made for the licensing of technology are expensed as research and development in the period in which they are incurred. Advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are delivered or the services are performed.

### **Research and Development and Pharmaceutical Drug Manufacturing Accruals**

The Company has entered into various contracts with third parties to perform research and development and pharmaceutical drug manufacturing. This includes contracts with contract research organizations ("CROs"), clinical manufacturing organizations ("CMOs"), testing laboratories, research hospitals and not for profit organizations and other entities to support our research and development activities. When billing terms under these contracts do not coincide with the timing of when the work is performed, the Company is required to make estimates of outstanding obligations to those third parties as of period end. The accrual estimates are based on a number of factors, including the Company's knowledge of the research and development programs and pharmaceutical drug manufacturing activities and associated timelines, invoicing to date, and the provisions in the contract. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from our estimates.

### **Patent Costs**

All patent-related costs incurred in connection with filing and prosecuting patent applications are recorded as general and administrative expenses as incurred.

### **Stock-Based Compensation**

The Company measures all stock options and other stock-based awards granted to employees at fair value on the date of grant. The Company uses the Black-Scholes option-pricing model in the valuation of its stock options. The fair value of restricted stock units with service-based and performance-based vesting is based on the fair value of the stock on the date of grant. The Company uses the Monte-Carlo model to calculate the fair value on the date of grant of market-based awards. The fair value of service-based awards is recognized as stock-based compensation expense over the requisite service period, which is generally the vesting period of the respective award. For awards with graded vesting, the straight-line method of expense recognition is applied to all awards with service-only based conditions. The Company uses the graded-vesting method to record the expense of awards with both service-based and performance-based vesting conditions, commencing once achievement of the performance condition becomes probable. The Company classifies stock-based compensation expense in the consolidated statements of operations in the same manner in which the award recipient's payroll costs are classified. The Company accounts for stock-based compensation expense related to forfeitures as the forfeitures occur.

### **Income Taxes**

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the financial statements or in the Company's tax returns. Deferred taxes are determined based on the difference between the financial reporting and tax basis of assets and liabilities using enacted tax rates in effect in the years in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in income tax expense.

The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes based upon the weight of available evidence, that it is more likely than not that all or a portion of deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. The realization of deferred tax assets is dependent upon the Company's ability to generate future taxable income during the periods in which those temporary differences become deductible. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

Uncertain tax positions represent tax positions for which reserves have been established. The Company accounts for uncertainty in income taxes recognized in the consolidated financial statements by applying a two-step process to determine the amount to be

recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more likely than not to be sustained, the tax position is then assessed to determine the amount of benefit to be recognized in the financial statements. The amount that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. Income tax expense includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

### Net Income (Loss) per Share

Basic net income (loss) per common share is computed by dividing the net income (loss) by the weighted average number of shares of common stock outstanding for the period. Diluted net income (loss) per common share is computed by dividing net income (loss) 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 and unvested restricted stock units. For periods in which the Company reported a net loss, diluted net loss per common share is the same as basic net loss per common share, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.

The Company reported net losses for each of the years ended September 30, 2022, 2021 and 2020. The Company excluded the following potential common shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect:

	Years Ended September 30,		
	2022	2021	2020
	(in thousands)		
Options to purchase common stock	3,993	3,852	3,262
Unvested rTSRUs	101	111	46
Unvested PSUs	101	111	46
Unvested restricted stock units	219	117	45

### Segment Data

The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. The Company is a biotechnology company focused on discovering and developing small molecule drugs, with an emphasis on treatments for viral infections. Revenue is generated exclusively from transactions occurring with partners located in the United States, and all assets are held in the United States.

### Comprehensive Income (Loss)

Comprehensive income (loss) includes net income (loss) as well as other changes in stockholders' equity that result from transactions and economic events other than those with stockholders. The Company's only element of other comprehensive income (loss) is unrealized gains and losses on available-for-sale marketable securities.

### Going Concern

In August 2014, the FASB issued ASU 2014-15, *Presentation of Financial Statements - Going Concern (Subtopic 205-40)* ("ASU 2014-15"). The Company adopted this standard as of September 30, 2017. The standard requires the Company to assess its ability to continue as a going concern one year beyond the date of filing and, in certain circumstances, provide additional footnote disclosures. Based on a detailed cash forecast incorporating current research and development activities and related spending plans, the Company believes that its current cash, cash equivalents and short-term and long-term marketable securities on hand at September 30, 2022 is sufficient to fund operations for at least the next twelve months beyond the date of issuance of these consolidated financial statements. The amount of capital available will depend on the Company's management of its existing cash, cash equivalents and short-term and long-term marketable securities, as well as the level of future royalties the Company earns under its agreement with AbbVie. If the Company should require financing beyond these resources to fund its research and development efforts, it may not be able to obtain financing on acceptable terms, or at all.

### Recently Adopted Accounting Pronouncements

In December 2019, the FASB issued ASU 2019-12, *Simplifying the Accounting for Income Taxes (Topic 740)*, which removes certain exceptions to the general principles in Topic 740 – Income Taxes and improves consistent application of and simplifies GAAP for other areas of Topic 740 by clarifying and amending existing guidance. This ASU became effective for the Company beginning October 1, 2021 and interim periods within that year. The adoption of the standard did not have a material impact on the Company's financial position or results of operations.

## Recently Issued Accounting Pronouncements

Accounting standards that have been issued or proposed by the FASB or other standards-setting bodies that do not require adoption until a future date are not expected to have a material impact on the Company's consolidated financial statements upon adoption.

## 3. Fair Value of Financial Assets and Liabilities

The following tables present information about the Company's financial assets and liabilities that were subject to fair value measurement on a recurring basis as of September 30, 2022 and 2021 and indicate the fair value hierarchy of the valuation inputs utilized to determine such fair value:

	Fair Value Measurements at September 30, 2022 Using:			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
<b>Assets:</b>				
Cash equivalents:				
Money market funds	\$ 13,905	\$ —	\$ —	\$ 13,905
Marketable securities:				
U.S. Treasury notes	91,328	—	—	91,328
Corporate bonds	—	76,411	—	76,411
Commercial paper	—	66,784	—	66,784
	<u>\$ 105,233</u>	<u>\$ 143,195</u>	<u>\$ —</u>	<u>\$ 248,428</u>
<b>Liabilities:</b>				
Series 1 nonconvertible preferred stock	\$ —	\$ —	\$ 1,423	\$ 1,423
	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 1,423</u>	<u>\$ 1,423</u>
	Fair Value Measurements at September 30, 2021 Using:			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
<b>Assets:</b>				
Cash equivalents:				
Money market funds	\$ 54,819	\$ —	\$ —	\$ 54,819
Marketable securities:				
U.S. Treasury notes	83,038	—	—	83,038
Corporate bonds	—	124,703	—	124,703
Commercial paper	—	87,471	—	87,471
	<u>\$ 137,857</u>	<u>\$ 212,174</u>	<u>\$ —</u>	<u>\$ 350,031</u>
<b>Liabilities:</b>				
Series 1 nonconvertible preferred stock	\$ —	\$ —	\$ 1,506	\$ 1,506
	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 1,506</u>	<u>\$ 1,506</u>

Cash equivalents at September 30, 2022 and 2021 consist of money market funds that are readily convertible to cash and with less than 90 days until maturity.

During the years ended September 30, 2022, 2021, and 2020, there were no transfers between Level 1, Level 2 and Level 3.

The fair value of Level 2 instruments classified as marketable securities were determined through third-party pricing services. The pricing services use many observable market inputs to determine value, including reportable trades, benchmark yields, credit spreads, broker/dealer quotes, bids, offers, and current spot rates.

The outstanding shares of Series 1 nonconvertible preferred stock as of September 30, 2022 and 2021 are measured at fair value. These outstanding shares are financial instruments that might require a transfer of assets because of the liquidation features in the contract and are therefore recorded as liabilities and measured at fair value. The fair value of the outstanding shares is based on significant inputs not observable in the market, which represent a Level 3 measurement within the fair value hierarchy. The Company utilizes a probability-weighted valuation model, which takes into consideration various outcomes that may require the Company to transfer assets upon liquidation. Changes in the fair values of the Series 1 nonconvertible preferred stock are recognized in other income (expense) in the consolidated statements of operations.

The recurring Level 3 fair value measurements of the Company's outstanding Series 1 nonconvertible preferred stock using probability-weighted discounted cash flow include the following significant unobservable inputs:

**Series 1 nonconvertible preferred stock**

Unobservable Input	Range September 30,	
	2022	2021
Probabilities of payout	0%-65%	0%-65%
Discount rate	7.25%	4.25%

The following table provides a rollforward of the aggregate fair value of the Company's outstanding Series 1 nonconvertible preferred stock for which fair value is determined by Level 3 inputs:

	Series 1 Nonconvertible Preferred Stock	
	(in thousands)	
<b>Balance, September 30, 2019</b>	\$	1,628
Decrease in fair value		(149)
<b>Balance, September 30, 2020</b>		1,479
Increase in fair value		27
<b>Balance, September 30, 2021</b>		1,506
Decrease in fair value		(83)
<b>Balance, September 30, 2022</b>	\$	1,423

**4. Marketable Securities**

As of September 30, 2022 and 2021, the fair value of available-for-sale marketable securities, by type of security, was as follows:

	September 30, 2022				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Credit Losses	Fair Value
	(in thousands)				
Corporate bonds	\$ 78,663	\$ —	\$ (2,252)	\$ —	\$ 76,411
Commercial paper	66,784	—	—	—	66,784
U.S. Treasury notes	92,416	—	(1,088)	—	91,328
	<u>\$ 237,863</u>	<u>\$ —</u>	<u>\$ (3,340)</u>	<u>\$ —</u>	<u>\$ 234,523</u>

	September 30, 2021				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Credit Losses	Fair Value
	(in thousands)				
Corporate bonds	\$ 124,678	\$ 93	\$ (68)	\$ —	\$ 124,703
Commercial paper	87,471	—	—	—	87,471
U.S. Treasury notes	83,061	3	(26)	—	83,038
	<u>\$ 295,210</u>	<u>\$ 96</u>	<u>\$ (94)</u>	<u>\$ —</u>	<u>\$ 295,212</u>

As of September 30, 2022 and 2021, marketable securities consisted of investments that mature within one year, with the exception of certain corporate bonds and U.S. Treasury notes, which have maturities between one and three years and an aggregate fair value of \$29,285 and \$108,416, respectively.



## 5. Property and Equipment, Net

Property and equipment, net consisted of the following as of September 30, 2022 and 2021:

	September 30,	
	2022	2021
	(in thousands)	
Laboratory and office equipment	\$ 14,780	\$ 14,499
Leasehold improvements	7,276	7,140
Purchased software	1,412	1,387
Furniture	1,354	1,294
Computer equipment	653	529
Construction in progress	2,556	20
	28,031	24,869
Less: Accumulated depreciation and amortization	(21,858)	(18,926)
	<u>\$ 6,173</u>	<u>\$ 5,943</u>

As of September 30, 2022, construction in progress related primarily to leasehold improvements. Depreciation and amortization expense for property and equipment, was \$2,973, \$3,334 and \$3,644 for the years ended September 30, 2022, 2021, and 2020, respectively.

## 6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following as of September 30, 2022 and 2021:

	September 30,	
	2022	2021
	(in thousands)	
Accrued pharmaceutical drug manufacturing	\$ 6,932	\$ 8,402
Accrued research and development expenses	5,532	6,062
Accrued payroll and related expenses	6,439	6,094
Accrued other	2,033	1,871
	<u>\$ 20,936</u>	<u>\$ 22,429</u>

## 7. Collaboration Agreements

### AbbVie Collaboration

The Company has a Collaborative Development and License Agreement (as amended, the “AbbVie Agreement”), with AbbVie to identify, develop and commercialize HCV NS3 and NS3/4A protease inhibitor compounds, including paritaprevir and glecaprevir, under which the Company has received license payments, proceeds from a sale of preferred stock, research funding payments, milestone payments and royalties totaling approximately \$1,207,000 through September 30, 2022. Since the Company satisfied all of its performance obligations under the AbbVie Agreement by the end of fiscal 2011, all milestone payments received since then have been recognized as revenue when the milestones were achieved by AbbVie.

The Company is receiving annually tiered royalties per Company protease product ranging from ten percent up to twenty percent, or on a blended basis from ten percent up to the high teens, on the portion of AbbVie’s calendar year net sales of each HCV regimen that is allocated to the protease inhibitor in the regimen. Beginning with each January 1, the cumulative net sales of a given royalty-bearing protease inhibitor product start at zero for purposes of calculating the tiered royalties on a product-by-product basis. The following table details the royalty tiers associated with cumulative calendar year net sales allocated to each royalty-bearing product as provided in the AbbVie Agreement:

Calendar Year Net Sales (in thousands)	Royalty Tier (%)
up to \$500,000	10%
from \$500,000 up to \$750,000	12%
from \$750,000 up to \$1,000,000	14%
from \$1,000,000 up to \$2,500,000	17%
greater than or equal to \$2,500,000	20%

Royalties owed to the Company under the agreement can be reduced by AbbVie in certain circumstances, including (i) if AbbVie exercises its right to license or otherwise acquire rights to intellectual property controlled by a third party where a product could not be legally developed or commercialized in a country without the third-party intellectual property right, (ii) where a product developed under the collaboration agreement is sold in a country and not covered by a valid patent claim in such country, and (iii) where sales of a generic product are equal to at least a specified percentage of AbbVie's market share of its product in a country.

AbbVie's obligation to pay royalties on a product developed under the agreement expires on a country-by-country basis upon the later of (i) the date of expiration of the last of the licensed patents with a valid claim covering the product in the applicable country, or (ii) ten years after the first commercial sale of the product in the applicable country.

Subject to certain exceptions, a party's rights and obligations under the agreement continue until (i) such time as AbbVie is no longer developing a product candidate or (ii) if, as of the time AbbVie is no longer developing any product candidates, AbbVie is commercializing any other protease inhibitor product, such time as all royalty terms for all covered products have ended. Accordingly, the final expiration date of the agreement is currently indeterminable.

Either party may terminate the agreement for cause in the event of a material breach, subject to prior notice and the opportunity to cure, or in the event of the other party's bankruptcy. Additionally, AbbVie may terminate the agreement for any reason upon specified prior notice.

If the Company terminates the agreement for cause or AbbVie terminates without cause, any licenses and other rights granted to AbbVie will terminate and AbbVie will be deemed to have granted the Company (i) a non-exclusive, perpetual, fully-paid, worldwide, royalty-free license, with the right to sublicense, under AbbVie's intellectual property used in any product candidate, and (ii) an exclusive (even as to AbbVie), perpetual, fully-paid, worldwide, royalty-free license, with the right to sublicense, under AbbVie's interest in any joint intellectual property rights to develop product candidates resulting from covered compounds and to commercialize any products derived from such compounds. Upon the Company's request, AbbVie will also transfer to the Company all right, title and interest in any related product trademarks, regulatory filings and clinical trials.

If AbbVie terminates the agreement for the Company's uncured breach, the milestone and royalty payments payable by AbbVie may be reduced, the licenses granted to AbbVie will remain in place, the Company will be deemed to have granted AbbVie an exclusive license under the Company's interest in joint intellectual property, AbbVie will continue to have the right to commercialize any covered products, and all rights and licenses granted to the Company by AbbVie will terminate.

## **8. Stockholders' Equity**

The Company is authorized to issue 100,000 shares of common stock at a par value of \$0.01 per share. Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are entitled to receive such dividends as may be declared by the board of directors, if any.

The Company also is authorized to issue 5,000 shares of preferred stock at a par value of \$0.01 per share, of which 2,000 shares are designated as Series 1 Nonconvertible preferred stock and 3,000 shares are undesignated and unissued.

## **9. Series 1 Nonconvertible Preferred Stock**

The Company's Certificate of Incorporation authorizes the issuance of up to 2,000 shares of Series 1 nonconvertible preferred stock at a par value of \$0.01 per share. Holders of Series 1 nonconvertible preferred stock are not entitled to receive dividends. In the event of any liquidation, deemed liquidation, dissolution or winding up of the Company, the Series 1 nonconvertible preferred stockholders are entitled to receive in preference to all other stockholders, an amount equal to \$1.00 per share, adjusted for any stock dividends, stock splits or reclassifications. Series 1 nonconvertible preferred stockholders will not be entitled to vote unless required by the Company pursuant to the laws of the State of Delaware. The Company may redeem the Series 1 nonconvertible preferred stock with the approval of the holders of a majority of the outstanding shares of Series 1 nonconvertible preferred stock at a redemption price of \$1.00 per share. The Company must redeem the stock within 60 days of such election. Shares that are redeemed will be retired or canceled and not reissued by the Company. As these shares qualify as a derivative, they are classified as a liability on the Company's consolidated balance sheet.

As of September 30, 2022 and 2021, 1,930 shares of Series 1 nonconvertible preferred stock were issued and outstanding. For the years ended September 30, 2022, 2021, and 2020, the remeasurement of the Series 1 nonconvertible preferred stock resulted in income (expense) of \$83, \$(27), and \$149, respectively, which was recorded in other income (expense) in the consolidated statements of operations. The total fair value of the Series 1 nonconvertible preferred stock was \$1,423 and \$1,506 as of September 30, 2022 and 2021, respectively.

## **10. Stock-Based Awards**

The Company grants stock-based awards, including stock options, restricted stock units and other unit awards under its 2019 Equity Incentive Plan (the "2019 Plan"), which was approved by its stockholders on February 28, 2019 and amended in March 2021 and March 2022. The Company also has outstanding stock option awards under its 2012 Equity Incentive Plan (the "2012 Plan") and its

amended and restated 1995 Equity Incentive Plan (the “1995 Plan”), but is no longer granting awards under these plans. The Company’s 2019 Plan permits the Company to sell or issue awards of common stock or restricted common stock or to grant awards of incentive stock options or nonqualified stock options for the purchase of common stock, restricted stock units, performance units, stock appreciation rights or other cash incentive awards, to employees, members of the board of directors and consultants of the Company. The number of shares of common stock that may be issued under the 2019 Plan is subject to increase by the number of shares forfeited under any options forfeited and not exercised under the 2019 Plan or any predecessor plans such as the 2012 Plan or the 1995 Plan. As of September 30, 2022, 1,363 shares remained available for future awards under the 2019 Plan.

Under the Company’s Employee Stock Purchase Plan (“ESPP”) a total of 186 shares of common stock are reserved for issuance. As of September 30, 2022, the Company had not commenced any offering under the ESPP and no ESPP shares have been issued.

Options granted under the 2019 Plan to employees generally vest over four years and to non-employee directors over one year, and expire after ten years. As required under the equity plans, the exercise price for awards granted is not to be less than the fair value of common shares on the date of grant. Restricted stock units with service-based vesting conditions generally vest over four years.

## Stock Option Valuation

The fair value of each stock option award is determined on the date of grant using the Black-Scholes option-pricing model. The volatility has been determined using the Company’s traded stock price to estimate expected volatility. The expected term of the Company’s options has been determined utilizing the “simplified” method for awards that qualify as “plain-vanilla” options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. The expected dividend yield is zero due to the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future. The relevant data used to determine the value of the stock option awards are as follows, presented on a weighted average basis:

	Years Ended September 30,		
	2022	2021	2020
Risk-free interest rate	1.72%	0.61%	1.41%
Expected term (in years)	6.04	6.05	6.02
Expected volatility	47%	52%	53%
Expected dividends	0%	0%	0%
Weighted average grant date fair value	\$ 33.22	\$ 21.76	\$ 30.47

The following table summarizes stock option activity, including aggregate intrinsic value for the year ended September 30, 2022:

	Shares Issuable Under Options (in thousands)	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term in years	Aggregate Intrinsic Value (in thousands)
<b>Outstanding as of September 30, 2021</b>	3,852	\$ 48.61	6.4	\$ 49,173
Granted	894	71.26		
Exercised	(517)	41.17		
Forfeited	(236)	66.76		
<b>Outstanding as of September 30, 2022</b>	<u>3,993</u>	\$ 53.57	6.2	\$ 28,778
<b>Options vested and expected to vest as of September 30, 2022</b>	<u>3,993</u>	\$ 53.57	6.2	\$ 28,778
<b>Options exercisable as of September 30, 2022</b>	<u>2,621</u>	\$ 49.76	5.0	\$ 25,191

The aggregate intrinsic value of options is calculated as the difference between the exercise price of the options and the fair value of the Company’s common stock. The following tables summarize additional exercise and grant date information:

	Years Ended September 30,		
	2022	2021	2020
		(in thousands)	
Aggregate intrinsic value of stock options exercised	\$ 17,650	\$ 2,704	\$ 7,850
Proceeds to Company from stock options exercised	\$ 21,262	\$ 3,614	\$ 10,481

## Market and Performance-Based Stock Unit Awards

The Company awards both performance share units (“PSUs”) and relative total stockholder return units (“rTSRUs”) to its executive officers.

The PSUs vest and result in issuance, or settlement, of common shares for each recipient, based upon the recipient's continued employment with the Company through the settlement date of the award and the Company's achievement of specified research and development milestones. The requisite service period of the PSUs is generally two years. The fair value of PSUs is based on the fair value of the stock on the date of grant, which is determined to be the closing price of the Company's common stock. Stock-based compensation expense for PSUs is recorded in the statements of operations over the service period, commencing when it is probable that the specified research and development milestone is achieved.

The rTSRUs vest and result in the issuance of common stock based upon the recipient's continuing employment with the Company through the settlement date of the award and the relative ranking of the total stockholder return, or TSR, of the Company's common stock in relation to the TSR of the component companies in the NASDAQ Biotech Index over two specified periods that are two years apart, based on a comparison of average closing stock prices in specified periods noted in the award agreement. The number of market-based rTSRUs awarded represents the target number of shares of common stock that may be earned; however, the actual number of shares that may be earned ranges from 0% to 150% of the target number, depending on the award agreement and the year of the award. The Company used a Monte Carlo model to estimate the grant-date fair value of the rTSRUs. Stock-based compensation expense for rTSRUs is recorded in the statements of operations over the service period regardless of whether the market condition is achieved.

Assumptions and estimates utilized in the calculation of the fair value of the rTSRUs include the risk-free interest rate, dividend yield, expected volatility based on the historical volatility of publicly traded peer companies and the remaining performance period of the award. The table below sets forth the weighted average grant date fair value assumptions used to value the rTSRUs:

	Years Ended September 30,		
	2022	2021	2020
Risk-free interest rate	0.94%	0.13%	1.62%
Dividend yield	0%	0%	0%
Expected volatility	80%	74%	68%
Performance period (years)	1.97	1.97	2.03

The following table summarizes PSU and rTSRU activity (at target) for the year ended September 30, 2022:

	PSUs		rTSRUs	
	Shares	Weighted Average Grant Date Fair Value per Share (in thousands, except per share data)	Shares	Weighted Average Grant Date Fair Value per Share
<b>Unvested at September 30, 2021</b>	111	\$ 49.31	111	\$ 31.26
Granted	36	76.84	36	54.67
Vested	(5)	61.59	(18)	40.13
Cancelled	(41)	59.01	(28)	37.78
<b>Unvested at September 30, 2022</b>	<u>101</u>	<u>\$ 54.50</u>	<u>101</u>	<u>\$ 36.14</u>

The total fair value of PSUs and rTSRUs vested during the years ended September 30, 2022, 2021, and 2020 were \$1,414, \$0 and \$1,227, respectively.

## Restricted Stock Units

The following table summarizes the restricted stock unit activity for the year ending September 30, 2022:

	Restricted Stock Units	Weighted Average Grant Date Fair Value per Share
	(in thousands, except per share data)	
<b>Unvested at September 30, 2021</b>	117	\$ 43.57
Granted	158	74.82
Vested	(29)	43.57
Cancelled	(27)	59.99
<b>Unvested at September 30, 2022</b>	<u>219</u>	<u>\$ 64.03</u>

The total fair value of restricted stock units vested during the years ended September 30, 2022, 2021, and 2020 were \$2,427, \$1,897 and \$3,149, respectively.

## Stock-Based Compensation Expense

The Company recorded the following stock-based compensation expense for the years ended September 30, 2022, 2021, and 2020:

	Years Ended September 30,		
	2022	2021	2020
	(in thousands)		
Research and development	\$ 9,728	\$ 10,075	\$ 10,096
General and administrative	17,241	10,916	9,479
	<u>\$ 26,969</u>	<u>\$ 20,991</u>	<u>\$ 19,575</u>

	Years Ended September 30,		
	2022	2021	2020
	(in thousands)		
Stock options	\$ 19,615	\$ 18,004	\$ 17,459
rTSRUs	1,597	1,537	1,216
PSUs	2,628	235	259
Restricted stock units	3,129	1,215	641
	<u>\$ 26,969</u>	<u>\$ 20,991</u>	<u>\$ 19,575</u>

As of September 30, 2022, the Company had an aggregate of \$55,346 of unrecognized stock-based compensation cost, which is expected to be recognized over a weighted average period of 2.4 years.



## 11. Leases

The Company has two real estate leases for properties located in Watertown, Massachusetts. The first lease, for office and laboratory space at 500 Arsenal Street, was effective in fiscal 2011 and was set to expire in September 2022 with an option to extend the lease term for an additional five years. On November 19, 2021, the Company exercised its option to extend the lease term for an additional five years through September 1, 2027. The option to extend the lease term was not included in the right-of-use asset and lease liabilities as it was not reasonably certain of being exercised. Therefore, the Company accounted for the extension as a modification and re-assessed the classification of the lease as an operating lease. The total remeasurement of the lease resulted in an increase in the right-of-use asset and lease liability of \$15,076 during the year ended September 30, 2022.

The second lease, for office space located at 400 Talcott Avenue, was effective September 2018 for a term of six years with two options to extend the lease term for an additional three years each. The options to extend the lease terms were not included in the right-of-use assets and lease liabilities as they were not reasonably certain of being exercised. In May 2022, the Company amended the lease to add additional office space and extend the lease term through June 1, 2034. The amended lease also includes a tenant improvement allowance from the landlord of up to \$2,574. The Company accounted for the lease amendment as a modification and re-assessed the classification of the lease as an operating lease. The total remeasurement of the lease resulted in an increase in the right-of-use asset and liability of \$8,174 during the year ended September 30, 2022.

Lease payments for the Company's real estate leases include fixed lease payments that escalate over the terms of the leases and require the Company to pay certain operating expenses based on actual costs incurred. Operating expenses that are not fixed in nature are expensed in the period incurred and included in variable lease costs. The leases do not include any restrictions or covenants that had to be accounted for under the lease guidance.

In May 2022, the Company entered into a new ten-year lease agreement with its existing landlord for laboratory and office space in Watertown, Massachusetts, adjacent to its 400 Talcott Avenue premises to accommodate its growing headcount. The new lab and office space will be located at Arsenal on the Charles in Watertown, Massachusetts, at a to-be-constructed facility. The Company expects to gain access to the space to perform tenant improvements beginning in October 2023. The estimated minimum lease payments as a result of the new lease total \$76,470 over the ten-year term. The lease also contains a tenant improvement allowance of \$15,194. The Company will account for the lease as a right-of-use asset and lease liability upon the lease commencement date.

In conjunction with the new lease agreement at Arsenal on the Charles, the Company amended its 500 Arsenal Street lease to shorten the term of the lease from September 2027 to the date when the Arsenal on the Charles facility is completed and ready for the Company's occupancy. The construction of the Arsenal on the Charles facility is being conducted by the landlord and it is expected that the facility will be ready for the Company's tenant improvement buildout in October 2023. As the construction of the facility and the timing of completion is not in the control of the Company, the Company will remeasure the term for the 500 Arsenal Street lease for financial accounting purposes at the time the contingency regarding occupancy lapses.

The Company leases units of equipment over eighteen-month lease periods commencing upon shipment of each unit. The lease agreements contain options to terminate the leases early or to extend the leases for successive six-month periods, however these options were not included in the right-of-use assets and lease liability as they were not reasonably certain of being exercised. The equipment leases require the Company to pay for certain consumable and peripheral equipment supplies based on actual costs incurred. As these costs are not fixed in nature, they are expensed in the period incurred and included in variable lease costs.

The components of lease expense for the Company's real estate and equipment leases were as follows:

	Years Ended September 30,	
	2022	2021
	(in thousands)	
Operating lease cost	\$ 6,294	\$ 5,861
Short-term lease cost	—	—
Variable lease cost	2,375	4,057
	<u>\$ 8,669</u>	<u>\$ 9,918</u>
	Years Ended September 30,	
	2022	2021
	(in thousands)	
Cash paid for amounts included in the measurement of operating lease liabilities	\$ 4,966	\$ 6,364
Operating lease liabilities arising from obtaining right-of-use assets	\$ 23,910	\$ 3,320
	September 30,	
	2022	2021
Weighted-average remaining lease term - operating leases (in years)	7.42	1.43
Weighted-average discount rate - operating leases	6.96%	6.08%

As the Company's leases do not provide an implicit rate, the Company utilized its incremental borrowing rate based on information available at the lease commencement date, which represents an internally developed rate that would be incurred to borrow, on a collateralized basis, over a similar term, an amount equal to the lease payments in a similar economic environment.

Future annual minimum lease payments relating to the Company's lease liabilities as of September 30, 2022 were as follows:

<b>Years ended September 30,</b>	<b>(in thousands)</b>
2023	2,290
2024	5,062
2025	5,216
2026	5,373
2027	5,196
Thereafter	11,912
Total future minimum lease payments	35,049
Less: imputed interest	(9,786)
Total operating lease liabilities	<u>\$ 25,263</u>

<b>Included in the balance sheet:</b>	<b>September 30,</b>	
	<b>2022</b>	<b>2021</b>
	<b>(in thousands)</b>	
Current operating lease liabilities	\$ 2,891	\$ 4,203
Operating lease liabilities, net of current portion	22,372	1,126
Total operating lease liabilities	<u>\$ 25,263</u>	<u>\$ 5,329</u>

The tables above do not include lease payments related to the Company's Arsenal on the Charles facility because as of September 30, 2022, the lease commencement date had not occurred. Additionally, the tables above do not include the impact of shortening the term for the 500 Arsenal Street Lease as the term date is contingent upon events not in the Company's control.

The Company is required to maintain security deposits of \$652 in connection with various of its real estate leases, which amounts are included in other long-term assets on the Company's consolidated balance sheets. In addition, the Company is required to maintain letters of credit for certain of its leases, collateralized by money market accounts of \$3,968, which amounts are classified as long-term restricted cash on the consolidated balance sheets.

## **12. Commitments and Contingencies**

### **Litigation and Contingencies Related to Use of Intellectual Property**

From time to time, the Company may become subject to legal proceedings, claims and litigation arising in the ordinary course of business. The Company currently is not a party to any threatened or pending litigation. However, third parties might allege that the Company or its collaborators are infringing their patent rights or that the Company is otherwise violating their intellectual property rights. Such third parties may resort to litigation against the Company or its collaborators, which the Company has agreed to indemnify. With respect to some of these patents, the Company expects that it will be required to obtain licenses and could be required to pay license fees or royalties, or both. These licenses may not be available on acceptable terms, or at all. A costly license, or inability to obtain a necessary license, would have a material adverse effect on the Company's financial condition, results of operations or cash flows. The Company accrues contingent liabilities when it is probable that future expenditures will be made and such expenditures can be reasonably estimated.

In June 2022, the Company announced that it filed suit in the United States District Court for the District of Massachusetts on June 21, 2022, against Pfizer, Inc. seeking damages for infringement of U.S. Patent No. 11,358,953 (the '953 Patent) in the manufacture, use and sale of Pfizer's COVID-19 antiviral, Paxlovid™ (nirmatrelvir tablets; ritonavir tablets). The United States Patent and Trademark Office awarded the '953 Patent to the Company in June 2022 based on the Company's July 2020 patent application describing coronavirus protease inhibitors invented by the Company. The Company is seeking fair compensation for Pfizer's use of a coronavirus protease inhibitor claimed in the '953 patent. The Company records all legal expenses associated with the patent infringement suit as incurred in the consolidated statements of operations.

The Company currently is not a party to any other litigation.

### **Indemnification Agreements**

In the ordinary course of business, the Company may provide indemnifications of varying scope and terms to customers, vendors, lessors, business partners, and other parties with respect to certain matters including, but not limited to, losses arising out of breach of

such agreements or from services to be provided to the Company, or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors and its executive officers that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. In addition, the Company maintains directors' and officers' insurance coverage. The Company does not believe that the outcome of any claims under indemnification arrangements will have a material effect on its financial position, results of operations or cash flows, and has not accrued any liabilities related to such obligations in its consolidated financial statements as of September 30, 2022 and 2021.

### 13. Income Taxes

Income before income taxes for all periods presented is from domestic operations, which are the Company's only operations. During the years ended September 30, 2022, 2021, and 2020, the Company recorded income tax benefit (expense) as follows:

	Years Ended September 30,		
	2022	2021	2020
	(in thousands)		
Current income tax benefit (expense):			
Federal	\$ —	\$ 28,721	\$ 8,491
State	449	205	941
Deferred income tax benefit (expense):			
Federal	(16)	(343)	(8,916)
State	—	—	(1,665)
Income tax benefit (expense)	<u>\$ 433</u>	<u>\$ 28,583</u>	<u>\$ (1,149)</u>

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective tax rate is as follows:

	Years Ended September 30,		
	2022	2021	2020
Federal statutory income tax rate	(21.0)%	(21.0)%	(21.0)%
State taxes, net of federal benefit	(2.9)	(2.3)	(2.8)
Change in valuation allowance	30.8	9.9	52.1
Federal research and development tax credit	(4.6)	(5.3)	(13.3)
Share-based compensation	(0.8)	2.4	2.8
State research and development tax credit	(1.5)	(0.8)	(2.6)
Change in deferred tax rate	(0.1)	(9.5)	(10.2)
Other	(0.3)	—	(1.7)
Effective income tax rate	<u>(0.4)%</u>	<u>(26.6)%</u>	<u>3.3 %</u>

The effective tax rate during the year ended September 30, 2022 differs from the U.S. federal statutory rate primarily due to the full valuation allowance maintained on the Company's net deferred tax assets. The negative effective income tax rate during the year ended September 30, 2021 reflects an income tax benefit due to the Company's ability to carryback the pre-tax loss for the year under the Coronavirus Aid, Relief and Economic Security Act ("CARES Act").

Changes in the valuation allowance for deferred tax assets during the years ended September 30, 2022, 2021, and 2020 are as follows:

	Years Ended September 30,		
	2022	2021	2020
	(in thousands)		
Valuation allowance, beginning of year	\$ (29,298)	\$ (18,259)	\$ —
Increase recorded to valuation allowance	(38,428)	(11,039)	—
Initial recording of valuation allowance	—	—	(18,259)
Valuation allowance, end of year	<u>\$ (67,726)</u>	<u>\$ (29,298)</u>	<u>\$ (18,259)</u>

Net deferred tax assets as of September 30, 2022 and 2021 consisted of the following:

	September 30,	
	2022	2021
	(in thousands)	
Deferred tax assets:		
Share-based compensation	\$ 14,983	\$ 11,843
Tax credit carryforwards	20,663	13,170
Operating lease liability	6,007	1,232
Accrued compensation	1,362	1,284
Net operating loss carryforward	29,105	3,095
Accrued expenses	541	378
Other temporary differences	245	366
Total deferred tax assets	72,906	31,368
Valuation allowance	(67,726)	(29,298)
Net deferred tax assets	5,180	2,070
Deferred tax liabilities:		
Operating lease, right-of-use assets	(5,606)	(1,110)
Depreciation	(88)	(684)
Prepaid expenses	(280)	(275)
Unrealized loss	794	(1)
Total deferred tax liabilities	(5,180)	(2,070)
Net deferred income tax assets (liabilities)	\$ —	\$ —

As of September 30, 2022, the Company had federal net operating loss carryforwards of \$109,363, which may be available to offset future taxable income and do not expire but are limited in their usage to an annual deduction equal to 80% of annual taxable income. As of September 30, 2022, the Company had state net operating loss carryforwards of \$97,128, which may be available to offset future taxable income and expire at various dates beginning in 2040. As of September 30, 2022, the Company also had federal and state research and development tax credit carryforwards of \$16,870 and \$4,986, respectively, which may be available to reduce future tax liabilities and expire at various dates beginning in 2039 and 2034, respectively.

Utilization of the federal and state net operating loss carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, and corresponding provisions of state law, due to ownership changes that may have occurred previously or that could occur in the future. These ownership changes may limit the amount of net operating loss and research and development tax credit carryforwards that can be utilized annually to offset future tax liabilities.

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets, which are comprised primarily of net operating loss carryforwards, research and development tax credit carryforwards and stock compensation expense. The Company considers it more likely that it will not have sufficient taxable income in the future that will allow it to realize all of its existing deferred tax assets. This is due to the fact the Company continues to progress its wholly-owned research and development programs and its declining royalty revenues from its Collaboration Agreement with AbbVie. As a result, the Company continued to record a valuation allowance as of September 30, 2022 against its deferred tax assets to reduce a portion of the Company's deferred tax assets for which the Company does not believe it is more likely than not these will be realized.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. The Company's tax years in the U.S. are still open under statute from 2018 to the present. Earlier years may be examined to the extent that tax credit or net operating loss carryforwards are used in future periods. The Company has not received notice of examination by any jurisdiction for any tax year open under statute.

In response to the COVID-19 pandemic, the CARES Act was signed into law in March 2020. The CARES Act lifted certain deduction limitations originally imposed by the Tax Cuts and Jobs Act of 2017 (the "Tax Act"). Under the CARES Act, the Company was permitted to carryback net operating losses for up to five years for losses generated in fiscal 2018 through fiscal 2021. Net operating loss carrybacks were previously prohibited under the Tax Act. The CARES Act also eliminated the 80% of taxable income limitations by allowing corporate entities to fully utilize net operating loss carryforwards to offset taxable income in fiscal years 2018, 2019 or 2020. In addition, the CARES Act made qualified improvement property eligible for 15-year cost-recovery and 100% bonus depreciation. The enactment of the CARES Act resulted in a \$28,721 and \$8,581 income tax benefit related to a federal net operating loss carryback at the previously enacted 35% rate in the Company's consolidated financial statements during the years ended

September 30, 2021 and 2020, respectively. As of September 30, 2022 and 2021, the Company had an income tax receivable of \$28,718 and \$37,255, respectively.

Uncertain tax positions represent tax positions for which reserves have been established. The Company's policy is to record interest and penalties related to uncertain tax positions as part of income tax expense. Total interest related to uncertain tax positions recorded as a liability on the Company's consolidated balance sheets were \$44 and \$105 as of September 30, 2022 and 2021, respectively. A reconciliation of the beginning and ending amount of uncertain tax positions is summarized as follows:

	September 30,	
	2022	2021
	(in thousands)	
<b>Beginning Balance</b>	\$ 622	\$ 844
Additions based on tax positions for the current period	10	10
Reductions for tax positions due to lapse of statute of limitations	(367)	(134)
Reductions for tax positions of prior periods	(39)	(98)
<b>Ending Balance</b>	<u>\$ 226</u>	<u>\$ 622</u>

The Company does not expect that its uncertain tax position will materially change within the next twelve months.

#### 14. 401(k) Plan

The Company has a 401(k) plan. This plan covers substantially all employees who meet minimum age and service requirements. During the years ended September 30, 2022, 2021, and 2020, the Company recognized \$1,596, \$1,353, and \$1,190, respectively, of expense related to its contributions to this plan.



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## MANAGEMENT TEAM

### Jay R. Luly, Ph.D.

President, Director and Chief Executive Officer

### Nathaniel S. Gardiner, J.D.

Senior Vice President and General Counsel

### Tara L. Kieffer, Ph.D.

Senior Vice President, New Product Strategy and Development

### Brendan Luu

Senior Vice President, Business Development

### Paul J. Mellett

Senior Vice President, Finance & Administration and Chief Financial Officer

### Yat Sun Or, Ph.D.

Senior Vice President, Research & Development and Chief Scientific Officer

### Scott T. Rottinghaus, M.D.

Senior Vice President and Chief Medical Officer

## BOARD OF DIRECTORS

### Bruce L. A. Carter, Ph.D.

Non-Executive Chairman of the Board, Enanta Pharmaceuticals, Inc.; Former President and Chief Executive Officer, ZymoGenetics, Inc.

### Mark G. Foletta

Former Chief Financial Officer, Amylin Pharmaceuticals, Inc., and other companies

### Yujiro S. Hata

Founder and Chief Executive Officer, IDEAYA Biosciences, Inc.

### Jay R. Luly, Ph.D.

President and Chief Executive Officer, Enanta Pharmaceuticals, Inc.

### Kristine Peterson

Former Chief Executive Officer, Valeritas, Inc.

### Lesley Russell, MBChB, MRCP

Former Chief Medical Officer, Cephalon, Inc., and other companies

### Terry C. Vance

Private consultant and former biotechnology venture capital investor

## Corporate Headquarters

Enanta Pharmaceuticals, Inc.  
500 Arsenal Street  
Watertown, MA 02472

## Investor Inquiries

Investor Inquiries (including requests for a copy of Enanta's Annual Report on Form 10-K, available free of charge) should be directed to:

Enanta Pharmaceuticals, Inc.  
500 Arsenal Street  
Watertown, MA 02472  
Attention: Investor Relations  
Phone: 617-607-0800  
Email: [ir@enanta.com](mailto:ir@enanta.com)

The 2022 Annual Report on Form 10-K and other investor information are available in the *Investors* section of Enanta's website at [www.enanta.com](http://www.enanta.com).

## Independent Registered Public Accounting Firm

PricewaterhouseCoopers LLP  
101 Seaport Boulevard, Suite 500  
Boston, MA 02210

## Corporate Counsel

Foley Hoag LLP  
Seaport West  
155 Seaport Boulevard  
Boston, Massachusetts 02210

## Transfer Agent

Computershare Investor Services  
462 South 4th Street, Suite 1600  
Louisville, KY 40202

## Stock Listing

NASDAQ Global Select Market: ENTA

## Web Site

[www.enanta.com](http://www.enanta.com)

**Enanta Pharmaceuticals, Inc.**

500 Arsenal Street  
Watertown, MA 02472

[www.enanta.com](http://www.enanta.com)