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 December 31, 2021

OR

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

Commission file number: 001-36500

CYMABAY THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**94-3103561**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
7575 Gateway Blvd, Suite 110 Newark, CA	**94560**
(Address of principal executive offices)	**(Zip Code)**

(510) 293-8800

(Registrant's telephone number, including area code)

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

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

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

None

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

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

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

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

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 Act). Yes ☐ No ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant based upon the closing price of its Common Stock on the Nasdaq Global Select Market on June 30, 2021, was $298,401,478. This excludes 426,196 shares of the registrant's Common Stock held by executive officers, directors and stockholders affiliated with directors outstanding at June 30, 2021. Exclusion of such shares should not be construed to indicate that any such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the registrant or that such person is controlled by or under common control with the registrant.

The number of shares of common stock outstanding as of February 28, 2022, was 84,677,939.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Proxy Statement for its 2022 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days after the registrant's fiscal year ended December 31, 2021, are incorporated by reference in Part III, Items 10-14 of this Annual Report on Form 10-K.

CYMABAY THERAPEUTICS, INC.
ANNUAL REPORT ON FORM 10-K
For the Year Ended December 31, 2021

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CAUTIONARY LANGUAGE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, that are subject to the "safe harbor" created by those sections. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "would," "expect," "plan," "anticipate," "believe," "estimate," "projected," "potential," "seek," "target," "goal," "intend," and similar expressions intended to identify forward-looking statements. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance, time frames or achievements to be materially different from any future results, performance, time frames or achievements expressed or implied by the forward-looking statements. We discuss many of these risks, uncertainties and other factors in this Annual Report on Form 10-K in greater detail under the heading "Risk Factors." Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements. Also, these forward-looking statements represent our estimates and assumptions only as of the date of this filing. You should read this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We hereby qualify our forward-looking statements by our cautionary statements. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

In addition, statements that "we believe" or "we expect" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based on information available to us as of the date of this report. While we believe that information provides a reasonable basis for these statements, that information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all relevant information. These statements are inherently uncertain, and readers are cautioned not to unduly rely on these statements.

RISK FACTOR SUMMARY

We are subject to a number of risks that if realized could materially harm our business, prospects, operating results, and financial condition. Some of the more significant risks and uncertainties we face include those summarized below. The summary below is not exhaustive and is qualified by reference to the full set of risk factors set forth in Item 1A of this Form 10-K "Risk Factors." Please carefully consider all of the information in this Form10-K, including the full set of risks set forth in the "Risk Factors" section, and in our other filings with the SEC before making an investment decision regarding CymaBay.

Risks Related to the COVID-19 Pandemic

- Our business may be adversely affected by the effects of theCOVID-19 pandemic, particularly the emergence of COVID-19 variants such as the Delta and Omicron variants, including those impacting our ability to enroll and conduct critical clinical trials such as RESPONSE, as well as impacts to our other development efforts, administrative personnel and third-party service providers.

Risks Related to Our Financial Condition and Capital Requirements

- We have incurred significant net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. We may need to raise additional equity and/or debt capital to fund our continued operations, including clinical trials and other product development. In the event we do not successfully raise sufficient funds to finance our product development activities, we will curtail our product development activities commensurate with the magnitude of the shortfall or our product development activities may cease altogether.

- Failure to remain in compliance with our obligations under the development financing agreement with Abingworth could lead to reduced funding under the agreement and/or the acceleration of potentially significant payments to Abingworth.
- Our ability to generate future revenues from product sales is uncertain and depends upon our ability to successfully develop, obtain regulatory approval for, and commercialize product candidates, including most importantly, seladelpar.
- Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Risks Related to Clinical Development and Regulatory Approval

- Drug development and obtaining and maintaining regulatory approval for drug products is costly, time-consuming, and highly uncertain.
- Serious complications or side effects in connection with the use or development of our product candidates could lead to delay or discontinuation of development of our product candidates.

Risks Related to Our Reliance on Third Parties

- Our manufacturing partners and other service providers, including CROs managing our clinical trials, may fail to perform adequately in their efforts to support the development, manufacture, and commercialization of our drug candidates and future products.

Risks Related to Commercialization of Our Product Candidates

- We have never successfully commercialized a product. If any of our product candidates receive marketing approval, they may nonetheless be unable to gain sufficient market acceptance by physicians, patients, health care payors and others in the medical community.
- If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenue.
- The commercial success of our products is subject to significant competition from products or product candidates that may be superior to, or more cost effective than, our products or product candidates.

Risks Related to Our Intellectual Property

- We may not be able to protect the confidentiality of our trade secrets, and our patents or other means of defending our intellectual property may be insufficient to protect our proprietary rights.
- Patents or proprietary rights of others may restrict our development, manufacturing, and/or commercialization efforts and subject us to litigation and other proceedings that could find us liable for damages.

Other Risks Factors – Risks Related to Employees, Information Technology, and Owning Our Common Stock

- Our business is dependent on our key personnel and will be harmed if we cannot recruit and retain leaders in our development, administrative, and commercial organizations.
- Significant disruptions of information technology systems or breaches of data security could adversely affect our business.
- Changes in and failures to comply with United States and foreign privacy and data protection laws, regulations and standards may adversely affect our business, operations and consolidated financial performance.
- Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

PART I

Item 1. Business

Overview

We are a clinical-stage biopharmaceutical company focused on developing and providing access to innovative therapies for patients with liver and other chronic diseases with high unmet medical need.

Our lead product candidate, seladelpar, is a potent and selective agonist of peroxisome proliferator activated receptor delta (PPARd), a nuclear receptor that regulates genes directly or indirectly involved in the synthesis of bile acids/sterols, metabolism of lipids and glucose, inflammation and fibrosis. We are focused on developing seladelpar for the treatment of primary biliary cholangitis (PBC), an autoimmune disease that causes progressive destruction of the bile ducts in the liver resulting in impaired bile flow (cholestasis) and inflammation.

We reported net losses of approximately $90.0 million and $51.0 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, we had cash, cash equivalents and marketable securities totaling $194.6 million, which we believe is sufficient, together with committed capital, to fund our current operating plan through 2023.

Strategy

Our goal is to become a leading biopharmaceutical company focused on developing and providing access to innovative therapies for patients with liver and other chronic diseases with high unmet medical need. Key elements of our strategy are to:

- Advance clinical development of seladelpar for patients with PBC,
- Strengthen our patent portfolio and other means of protecting exclusivity, and
- Develop other product candidates.

Phase 3 Trials

We are in the process of enrolling a global, Phase 3 registration study (RESPONSE) to evaluate seladelpar in patients with PBC and currently anticipate completing enrollment in RESPONSE during the first half of 2022. We are also continuing the enrollment of a global long-term safety study (ASSURE) to evaluate seladelpar in patients with PBC.

CymaBay Pipeline Overview

Our pipeline includes two clinical stage product candidates: seladelpar (a PPARd agonist) and MBX-2982 (a GPR119 agonist).

Product Candidates	Disease/condition	Status	Description
Seladelpar (PPARd agonist)	Primary Biliary Cholangitis (PBC)	Phase 3	Ongoing 52-week Phase 3 study to evaluate seladelpar in PBC patients with inadequate response or intolerance to ursodeoxycholic acid (UDCA) (RESPONSE)
Seladelpar (PPARd agonist)	Nonalcoholic Steatohepatitis (NASH)	Phase 2b	Completed 52-week Phase 2b study to evaluate safety, tolerability, and effect of seladelpar in patients with NASH
MBX-2982 (GPR119 agonist)	Hypoglycemia in Type 1 Diabetics	Phase 2a	Ongoing proof-of-pharmacology Phase 2a study*

* Being conducted and funded by third parties (see MBX-2982 section below)

Seladelpar (MBX-8025)

Summary

Seladelpar is a selective agonist for the peroxisome proliferator-activated receptor delta (PPARd). The PPARd receptor is a nuclear receptor that regulates genes involved in bile acid/sterol, lipid, and glucose metabolism, and regulation of certain inflammatory cells. Seladelpar has the potential to treat certain diseases of the liver and a variety of disorders of lipid metabolism.

Seladelpar was initially developed for treatment of mixed dyslipidemia, which is characterized by elevated low-density lipoprotein (LDL-C) and triglycerides (TGs). Results from our Phase 2 clinical study of seladelpar in patients with mixed dyslipidemia established effects that we believe have the potential to benefit patients affected with PBC and other conditions. These benefits include:

- Reductions in LDL-C and total cholesterol, and increases in high-density-lipoprotein (HDL-C),
- Reductions in triglycerides and free fatty acids,
- Reductions in high-sensitivity C-reactive protein (hs-CRP), a marker of inflammation, and
- Reductions in alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT).

In February 2019, the Food and Drug Administration (FDA) granted seladelpar Breakthrough Therapy Designation for the treatment of early stage PBC, and in October 2016, seladelpar received the European Medicines Agency (EMA) PRIority MEdicines (PRIME) designation for the treatment of PBC. In November 2016, the FDA granted orphan drug designation to seladelpar for the treatment of PBC. In September 2017, EMA's Committee for Orphan Medicinal Products (COMP) granted orphan drug designation to seladelpar for the treatment of PBC.

To date, we have completed six-month and twelve-month toxicity studies of seladelpar in rats and monkeys, respectively, as well as two-year carcinogenicity studies in mice and rats. In addition, we have completed multiple Phase 1 clinical studies, three Phase 2 and one Phase 3 clinical study (ENHANCE) of seladelpar in PBC. In addition, we are in the process of conducting a second Phase 3 study (RESPONSE) with seladelpar in PBC. We believe that the data from the Phase 2 studies and the ENHANCE Phase 3 study established seladelpar's anti-cholestatic and anti-inflammatory effects and identified a dose (10 mg/day) that has the potential to offer patients improved efficacy and better tolerability over the only approved second-line treatment available today. Those studies showed reductions in markers of cholestasis including ALP and GGT, and showed improved inflammatory and metabolic markers with patients experiencing decreases in levels of transaminases, hs-CRP, and LDL-C. Many PBC patients suffer from pruritus, or itching, which can significantly impact their quality of life. Based on data from our Phase 2 and Phase 3 studies, and unlike the only approved second-line treatment currently available, we believe that seladelpar may reduce the incidence of pruritus in PBC patients.

Target Indications for Seladelpar

We are actively pursuing PBC as our initial launch indication for seladelpar. We may look to develop seladelpar in other indications in the future. Following is a review of PBC and NASH and our development progress for seladelpar in each indication.

Primary Biliary Cholangitis (PBC)

Summary

PBC is a rare, chronic progressive autoimmune liver disease that predominantly affects middle-aged women. A T-cell mediated immune response is thought to damage, and ultimately destroy, the interlobular and septal bile ducts. The loss of bile duct function leads to decreased bile secretion and retention of toxic substances, including bile acids, within the liver parenchyma. This retention may ultimately cause liver cirrhosis and liver failure in PBC patients.

PBC primarily affects an estimated one in 1,000 women over the age of 40. Due to its low prevalence, PBC has been recognized as an orphan disease in the U.S. and E.U., meeting their respective FDA and EMA orphan designation criteria. Diagnosis of PBC is confirmed by elevated serum ALP presence and/or the magnitude of antimitochondrial antibody (AMA presence), and liver biopsies, although biopsies are not required for diagnosis in most patients.

The most common clinical symptoms of PBC include fatigue and pruritus, or itching (up to 70% occurrence), which adversely affects many patients' quality of life. PBC patients are also frequently affected by conditions including jaundice, hyperlipidemia (notably hypercholesterolemia), hypothyroidism, osteopenia and osteoporosis, and coexisting autoimmune diseases. Late complications of PBC include portal hypertension, malabsorption, deficiencies of fat-soluble vitamins, and steatorrhea (excess fat in feces). Left untreated, PBC disease progression can lead to the need for liver transplantation and liver-related mortality. Despite being a rare disease, PBC is one of the top six indications for liver transplantation in the U.S. and E.U. Recurrence of PBC following liver transplantation is reported in 11-46% of transplantations, with an estimated prevalence of 30% at 10 years following transplantation, further demonstrating a need for effective therapies.

Retrospective analyses of PBC clinical outcomes data have shown that elevated levels of ALP and bilirubin are associated with worsened clinical outcomes including liver transplantation and death associated with PBC. These analyses supported the use of ALP and bilirubin as elements of a clinical surrogate reasonably likely to predict outcomes that was used for the approval of obeticholic acid as a second line therapy for PBC. The current first line therapy for PBC is ursodeoxycholic acid (UDCA), a secondary bile acid.

Studies of Seladelpar in PBC

RESPONSE (Phase 3)

We are currently enrolling patients in a global, Phase 3 registration study (RESPONSE) to evaluate seladelpar in patients with PBC. The Phase 3 study is a 52-week, double blind, placebo-controlled, randomized, global, registration study evaluating the safety and efficacy of seladelpar in patients with PBC. The study is intended to enroll 180 patients, who have an inadequate response to, or intolerance to, UDCA, in a 2:1 randomization to oral, once daily seladelpar 10 mg or placebo. The primary outcome measure will be the composite biochemical responder rate at 52 weeks. A responder is defined as a patient who achieves an ALP level less than 1.67 times the upper limit of normal with at least a 15% decrease from baseline and has a normal level of total bilirubin. Additional key outcomes of efficacy will compare the rate of normalization of ALP at 52 weeks and the change from baseline in level of pruritus at six months for patients with moderate to severe pruritus at baseline assessed by a numerical rating scale (NRS) recorded with an electronic diary.

ENHANCE (Phase 3)

In October 2018 we commenced a global, Phase 3 registration study (ENHANCE) to evaluate seladelpar in patients with PBC. The Phase 3 study was a double-blind, randomized, placebo-controlled 52-week study evaluating the safety and efficacy of 5 mg and 10 mg of seladelpar versus placebo in patients with PBC who had an inadequate response to, or were intolerant to, first-line treatment with UDCA.

Approximately 265 patients were randomized to receive placebo, 5 mg of seladelpar, or 10 mg of seladelpar. Patients on 5 mg could potentially increase their dose, in a double-blinded manner, to 10 mg after 6 months if they had not yet met the composite biochemical response criteria. The primary endpoint was a composite response defined as a patient achieving an ALP level below 1.67 times the upper limit of normal, with at least a 15% reduction from baseline, and a normal total bilirubin at 52 weeks. The primary efficacy analysis was to compare response rates of treatment groups to those of the placebo group. Key secondary endpoints were the ALP normalization rate and changes from baseline in pruritus, as measured by NRS in patients with moderate-to-severe pruritus at baseline.

In December 2019 we terminated ENHANCE early based on initial histological observations obtained in our Phase 2b study of seladelpar in NASH. In May 2020, we announced completion of an independent expert panel review into the NASH findings that concluded the data, in aggregate, did not support liver injury related to seladelpar. In June 2020, we discussed the data, the panel's conclusions, and other matters with the FDA. In July 2020, the FDA lifted the clinical hold on the program and we made the decision to reinstate clinical development of seladelpar in PBC.

In August 2020 we announced positive results from ENHANCE, which we believe support seladelpar as a safe, well-tolerated, and efficacious treatment for patients with PBC. Although the study was terminated prior to the completion of the 52-week treatment period, the statistical analysis plan was amended while the study remained blinded to adjust for evaluation of the primary and two key secondary endpoints at Week 12 rather than Week 52. Topline data for patients through 12 and to 26 weeks showed what we believe to be robust anti-cholestatic, anti-inflammatory and anti-pruritic activity of seladelpar. Specifically, 78.2% of patients on 10 mg of seladelpar compared with 12.5% on placebo achieved the primary composite outcome after 3 months ($p<0.0001$), and 27.3% of patients on 10 mg of seladelpar compared with 0% on placebo normalized ALP by 3 months ($p<0.0001$). In addition, the study revealed statistically significant improvement in change from baseline in pruritus at 3 months ($p<0.05$) for patients with moderate-to-severe itch treated with seladelpar 10 mg versus placebo.

Safety Studies

Prior to the decision to terminate in December 2019, we were conducting a long-term safety study of seladelpar, which was open to patients who had participated in other company-sponsored PBC studies. Patients completing the Phase 2 open label study discussed immediately below, as well as ENHANCE, were able to transfer into the long-term safety study. As of the time of termination, 106 patients had received seladelpar for at least 12 months and 51 patients had received seladelpar for at least 24 months. The safety study was discontinued due to the histological observations in the Phase 2b NASH study.

With the reinstatement of the clinical development of seladelpar we commenced a long-term safety study (ASSURE), which is open to patients who were eligible for the prior long-term extension study, including those from our Phase 2 open label study and our Phase 3 ENHANCE study, as well as patients completing treatment in RESPONSE. The ASSURE trial is ongoing and has already enrolled over 120 patients, with additional patients expected to enroll from prior seladelpar PBC trials as well patients completing treatment in RESPONSE.

Phase 2 Open Label Study

In December 2016, we initiated a Phase 2 study of seladelpar in patients with PBC. The study was an open label, randomized, dose-ranging study evaluating 2 mg, 5 mg and 10mg doses of seladelpar and the primary efficacy endpoint was percent change in ALP from baseline. The study had an initial twelve-week period in which starting doses were maintained, but after which doses could be increased to as high as 10 mg for those patients in which a greater biochemical response was deemed appropriate, these being described as titration groups. Secondary outcomes were to evaluate other markers of cholestasis, inflammation, and lipid parameters, as well as clinical symptoms such as pruritus and quality of life.

In November 2018 we announced data that we believe showed that seladelpar treatment led to sustained anti-cholestatic and anti-inflammatory effects with no worsening of pruritus through 52 weeks. Specifically, at 52 weeks the mean decreases in ALP were -47% and -46% in the 5/10 titration and 10 mg groups, respectively. A key secondary outcome was the composite response measured at week 52 where a responder was defined as a patient with ALP <1.67 x ULN, ≥15% decrease in ALP, and total bilirubin ≤ULN. At 52 weeks 59% and 71% of patients met the composite endpoint in the 5/10 titration and 10 mg groups, respectively. The anti-cholestatic effect of seladelpar was further substantiated with ALP normalization at 52 weeks in 24% and 29% of patients in

the 5/10 titration and 10 mg groups, respectively. Treatment with seladelpar also demonstrated a robust anti-inflammatory activity with median transaminase decreases of -31% and -33% in the 5/10 titration and 10 mg groups, respectively.

We subsequently reported on a 52-week analysis from the study on the effect of seladelpar on pruritus, or itching, which is a common clinical symptom of PBC that adversely effects a patient's quality of life. Patient self-reported experiences were collected using the pruritus visual analogue scale (VAS) in 101 PBC patients in the 5/10 titration or 10 mg groups. In patients with moderate to severe pruritus (VAS ≥ 40), substantial improvement in pruritus (VAS ≥ 20-point decrease) was seen in 58% and 93% of patients in the 5/10 titration and 10 mg groups, respectively. These data suggest that seladelpar is not associated with drug-induced pruritus and supported further evaluation of seladelpar's potential benefit on pruritus.

Of the 119 patients that received at least one dose of seladelpar (2, 5 or 10 mg), 11 serious adverse events were documented, and none were considered related to seladelpar. Three patients discontinued seladelpar, of which only one discontinuation, for a grade 1 gastroesophageal reflux, was deemed related to seladelpar. There was no transaminase safety signal, and importantly, there was no indication that seladelpar was associated with drug-induced pruritus.

Nonalcoholic Steatohepatitis (NASH)

Summary

Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease worldwide and encompasses a spectrum of conditions that arise from fat accumulation in the liver of individuals that cannot otherwise be attributed to alcohol consumption. The prevalence of NAFLD has increased and is reported to account for approximately 25% of the general population worldwide. It is widely believed that the increase in NAFLD prevalence is a consequence of the obesity epidemic, and studies associate NAFLD with visceral obesity, Type 2 diabetes, hypertension, dyslipidemia, and hypothyroidism.

The accumulation of fat in combination with hepatic inflammation can cause chronic liver injury leading to nonalcoholic steatohepatitis (NASH). NASH is the progressive form of NAFLD and increases patient risk of developing advanced liver fibrosis, cirrhosis, decompensated cirrhosis, the need for liver transplantation, hepatocellular carcinoma (HCC), and/or death. Serum markers that are often elevated in NASH patients include the transaminases alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST). Liver biopsies are performed to confirm a NASH diagnosis. Approximately 10-20% of individuals with NAFLD progress to NASH.

NASH Phase 2b Seladelpar Study

In May 2018, we initiated a randomized, placebo-controlled, parallel, dose-ranging Phase 2b study to evaluate seladelpar in patients with NASH. In February 2019, we announced full enrollment of 181 patients with liver biopsy proven NASH at specialized U.S. investigational centers. Seladelpar at doses of 10, 20, and 50 mg per day were studied versus placebo in a 2:2:2:1 randomization. The primary efficacy outcome was the change from baseline in liver fat content at 12 weeks as measured by magnetic resonance imaging using the proton density fat fraction method (MRI-PDFF). In June 2019, we announced results from the primary efficacy outcome, which were that treatment with seladelpar resulted in significant reductions in liver fat but that these changes were not significant when compared to placebo, which also had significant reductions. Treatment with seladelpar did, however, result in robust and clinically meaningful reductions in markers associated with liver injury. Alanine aminotransferase (ALT) declined up to 37.5% or 32 U/L in 12 weeks. These reductions in ALT are significantly greater than the 17 U/L threshold that has been correlated with histologic improvement in NASH. Gamma glutamyl transferase (GGT) also decreased significantly, suggesting a reduction in hepatocellular oxidative stress. Significant reductions in alkaline phosphatase (ALP) at 12 weeks were observed, supportive of a decrease in hepatocellular bile acids. The marked changes in these liver enzymes collectively suggested the potential to impact ballooning and lobular inflammation, the two key components of NASH resolution. In

November 2019, we announced that this trial was terminated based on initial histological observations. Although these patients had stable or improving biochemical markers of liver disease, we halted dosing of patients with seladelpar due to the lack of understanding the significance of the observations, and possible impact on patients.

In March 2020, we announced additional preliminary data from the terminated Phase 2b study of seladelpar in patients with NASH. For liver tests at 52 weeks, there were 19, 35, 41 and 40 evaluable patients in the placebo, 10, 20 and 50 mg groups, respectively. The corresponding percent changes from baseline at week 52 in ALT were +1.1%, -29.1%, -41.9% and -41.3%. Similarly for AST, relative changes at week 52 were-0.5%, -19.7%, -25.0%, and -16.6% percent for placebo, 10, 20 and 50 mg, respectively. Finally, corresponding changes in GGT were-0.6%, -29.0%, -46.1% and -35.0%. Out of 181 patients enrolled in the study, there were 152 with paired biopsies at entry and end-of-treatment. The number of patients with paired biopsies in the placebo, 10, 20 and 50 mg seladelpar groups were 25, 39, 42 and 46, respectively. The proportion of responders with resolution of NASH with no worsening in fibrosis were 8.0%, 10.3%, 19.0% and 26.1% in the placebo, 10, 20 and 50 mg seladelpar groups, respectively. The corresponding responder rates for at least a one stage improvement in fibrosis with no worsening in NASH were 20.0%, 23.1%, 23.8% and 37.0%. The proportion of patients meeting both endpoints were 8.0%, 5.1%, 11.9% and 19.6% for the placebo, 10, 20 and 50 mg seladelpar groups, respectively.

NASH Histology Review

In November 2019, we announced the termination of our Phase 2b study of seladelpar in subjects with NASH. In addition, we placed all studies of seladelpar in subjects with PBC on hold. The decision to halt development of seladelpar was based on initial histological observations in the Phase 2b study of seladelpar in NASH that were observed in the first blinded tranche of end-of-treatment liver biopsies in the trial. These observations were characterized by an interface hepatitis presentation, with or without biliary injury, and sometimes with the presence of numerous immune cells. Although these patients had stable or improving biochemical markers of liver disease, the decision to halt development was based on a need to understand the significance of the observations, and possible impact on patients, before dosing additional patients with seladelpar. The FDA agreed with this decision and subsequently placed a formal clinical hold on seladelpar in December 2019. Thereafter, we terminated all our ongoing clinical studies of seladelpar pending further investigation of the histological observations.

With the receipt of additional requests from the FDA, we initiated a series of investigative actions to better understand the baseline characteristics of patients enrolled in our Phase 2b NASH study and the histological observations identified by our study pathologists at the end of treatment. The investigation included three activities intended to confirm and subsequently understand the significance of the observations. The first was a comprehensive collection and review of data including patient demographics, medical history, concomitant medications and additional biochemical markers. The second was a blinded, independent review of baseline and end of treatment biopsies by several experienced liver pathologists. Finally, the third was a formal pathology and clinical hepatology review panel meeting during which experts reviewed all information gathered to provide a consensus independent determination of the role of seladelpar in these findings. These activities were essential to our follow-up with the FDA and to determine if there was a path forward for seladelpar.

In May 2020, we announced completion of the independent expert panel review into the findings from our NASH Phase 2b study. The eight-person panel included three hepatopathologists and five hepatologists with expertise in drug-induced liver injury, NASH and PBC. The expert panel found no clinical, biochemical or histological evidence of seladelpar-related liver injury in the study. The panel also unanimously supported the lifting of the clinical hold and the re-initiation of clinical development. In June 2020, we discussed the data, the panel’s conclusions, and other matters with the FDA and submitted a complete response letter to answer outstanding FDA questions and seek approval from the FDA to lift the clinical hold. In July 2020, we received a response from the FDA lifting the clinical hold, thereby permitting us to reinstate clinical development of seladelpar.

MBX-2982

MBX-2982 targets G protein-coupled receptor 119 (GPR119), a receptor that interacts with bioactive lipids known to stimulate glucose-dependent insulin secretion. Preclinical data indicate that MBX-2982 is a potent selective orally-active GPR119 agonist that functions through a unique dual mechanism of action that acts directly on the beta cell to increase insulin secretion and stimulates release of the incretin GLP-1 from the gut. We have previously conducted clinical studies for MBX-2982 as a potential treatment for diabetes, demonstrating MBX-2982 was, we believe, safe and well tolerated.

We believe MBX-2982 may also have utility in various diseases impacting the gut, liver or gut-liver axis and are currently exploring potential opportunities to advance development.

In November 2020, we announced a study to evaluate the potential for MBX-2982 to stimulate the release of the hormone glucagon in response to hypoglycemia in patients with type 1 diabetes (T1D). Glucagon is a regulatory hormone that elevates blood sugar levels in response to below normal glucose levels (hypoglycemia). Insulin-induced hypoglycemia in diabetes is a significant limiting factor in achieving the desired glucose control and is the cause of significant morbidity. In recent preclinical studies, GPR119 agonists were shown to enhance glucagon secretion in response to low glucose levels and were able to prevent hypoglycemia in animal models. The Phase 2a proof-of-pharmacology study will assess whether MBX-2982 can enhance glucagon secretion during insulin-induced hypoglycemia in subjects with T1D. If successful, studies to evaluate MBX-2982 as a potential preventive therapy for hypoglycemia in patients with T1D may be warranted. The study is being led by the AdventHealth Translational Research Institute in Orlando, Florida and is fully funded by The Leona M. and Harry B. Helmsley Charitable Trust. CymaBay retains full commercial rights to MBX-2982. The study is ongoing.

CB-0406

In 2020 we began to evaluate CB-0406, the active metabolite of the arhalofenate, a pro-drug previously studied for chronic metabolic diseases. We initiated a single and multiple ascending dose study of CB-0406 in healthy subjects to establish its pharmacokinetics, safety and maximum tolerated dose. While the study showed CB-0406 had improved pharmacokinetics versus arhalofenate, CB-0406's safety profile did not support continued development as a result of the occurrence of a small number of reversible cases of thrombocytopenia at higher doses. Therefore, in mid-2021 we discontinued development of CB-0406.

COVID-19 Pandemic

Through the date of filing of this Annual Report, the biggest impact of the COVID-19 outbreak on our operations, financial condition and liquidity has been the remote operation of our operations personnel and what we believe to be slower enrollment timelines for our RESPONSE trial. As a result of the continuing COVID-19 pandemic, we may experience future disruptions that could impact these and additional aspects of our business, including our progress towards the completion of our clinical studies, and other associated development activities. Possible disruptions are currently difficult to foresee. We continue to monitor areas of potential risk, which include but are not limited to the following:

- *Remote workforce operations*. During the pandemic to date, our workforce has adapted to remotely working to maintain operations. Our reliance on personnel working from home could potentially negatively impact future productivity, or disrupt, delay, or otherwise adversely impact our business. In addition, remote operations could increase our cyber-security and data privacy risks, create data accessibility concerns, and make us more susceptible to communication disruptions, any of which could adversely impact our business operations, or delay necessary interactions with regulators, contract manufacturers, contract research organizations, clinical trial sites, and other important agencies and contractors, which may result in increased costs to us.

- *Clinical trial and drug manufacturing operations*. In collaboration with our clinical research organization partners, we sponsor clinical trials that take place at investigator sites in the U.S. and internationally. We also partner with contract manufacturing organizations to develop, manufacture, and distribute our product candidate drug supplies. To date, these collective research and development personnel and vendors are adapting to COVID-19 related travel restrictions and reduced access to work facilities through the use of remote working technologies and other measures as they continue to progress toward enrollment and completion of our existing clinical trials. However, in the future, as we look to enroll and complete the clinical development of seladelpar and initiate other programs, our research and development employees and contractors may not be able to sufficiently access their applicable work facilities as a result of continued facility closure orders and the possibility that governmental authorities might further modify such restrictions. Furthermore, patients we expect to enroll in our clinical trials may also be impacted by any ongoing travel and facility access restrictions. Although we and our contractors continue to plan for and develop pandemic-related risk mitigation strategies, it is uncertain whether these plans will continue to be sufficient to fully offset the potential impact that travel and facility access restrictions (or other unanticipated impediments) may have on our ability to execute our development activities in a timely and cost-effective manner.
- *Drug regulator interactions.* The FDA, comparable foreign regulatory agencies, and ethics boards may experience operational interruptions or delays, which could impact timelines for regulatory meetings, submissions, trial initiations, and regulatory approvals.
- *Financial reporting and compliance*. To date, there has been no adverse impact on our ability to maintain our established financial reporting functions and internal controls over financial reporting. However, our ability to prepare our financial results timely and accurately is partially dependent upon the availability of third-party information systems and other cloud-based services. Any degradation in the quality or timeliness of critical third-party information or cloud-based services could adversely impact our financial reporting capabilities.

Overall, we cannot at this time predict the specific extent, duration, or full impact that the continuing COVID-19 pandemic will have on our financial condition and operations. The impact of the COVID-19 pandemic on our company will depend on future developments, including the duration and spread of the outbreak and related governmental advisories and restrictions. These developments and the impact of COVID-19 on the financial markets and the overall economy are highly uncertain. If the financial markets and/or the overall economy are impacted for an extended period, this may negatively impact our business.

License Agreements and Intellectual Property

General

We actively seek to obtain, where appropriate, patent protection and regulatory exclusivity for the proprietary technology that we consider important to our business, including compounds, compositions and formulations, their methods of use and processes for their manufacture both in the United States and other countries. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing to develop and maintain our proprietary position. Our success depends in part on our ability to obtain, maintain and enforce proprietary protection for our product candidates, technology and know-how, to operate without infringing the proprietary rights of others, and to exclude others from infringing our proprietary rights. However, patent protection may not afford us complete protection against competitors who seek to circumvent our patents.

We also depend upon the skills, knowledge, experience and know-how of our management, research and development personnel, as well as that of our advisors, consultants and other contractors. To help protect our proprietary know-how, which is not patentable, and for inventions for which patents may be difficult to enforce, we currently rely, and will in the future rely, on trade secret protection and confidentiality agreements to protect our interests. To this end, we require all of our employees, consultants, advisors and other contractors to enter

into confidentiality agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

Finance and Licensing Agreements

Our current significant finance and licensing arrangements are summarized below:

Johnson & Johnson: In June 2006, we entered into a license agreement with Janssen Pharmaceutical NV (Janssen NV), an affiliate of Johnson & Johnson, in which we received an exclusive worldwide, royalty-bearing license to seladelpar and certain other PPARd compounds (the PPARd Products) with the right to grant sublicenses to third parties to make, use and sell such PPARd Products. Under the terms of the agreement, we have full control and responsibility over the research, development and registration of any PPARd Products and are required to use diligent efforts to conduct all such activities. Janssen NV has the sole responsibility for the preparation, filing, prosecution, maintenance of, and defense of certain patents related to the PPARd Products. Janssen NV has a right of first negotiation under the agreement to license PPARd Products from us in the event that we elect to seek a third-party corporate partner for the research, development, promotion, and/or commercialization of such PPARd Product. Under the terms of the agreement Janssen NV is entitled to receive up to an 8% royalty on net sales of PPARd Products. Under the terms of the agreement, if we do not expend more than a de minimis amount of effort and resources on the research and/or development of at least one PPARd Product, such action would constitute a default under the agreement. In addition, if we fail to use diligent efforts to promote, market and sell any PPARd Product under the agreement, such action would constitute a default under the agreement. In the event of such default, or upon our termination of the agreement, we are obligated to grant Janssen NV a worldwide, exclusive, irrevocable license under the agreement in all information that is controlled, developed or acquired by us that relates to a PPARd compound or PPARd Product and in all patents that are filed during the term of the agreement with a priority date after the effective date of the agreement and relate to a PPARd compound or PPARd Product.

In June 2010, we entered into two development and license agreements with Janssen Pharmaceuticals, Inc. (Janssen), an affiliate of Johnson & Johnson, under which Janssen obtained the right to further develop undisclosed metabolic disease target agonists for the treatment of Type 2 diabetes and other disorders, and we received a one-time nonrefundable technology access fee related to the agreements. These development and licensing agreements were terminated as of April 2015. In December 2015, we exercised an option pursuant to the terms of one of the original agreements to continue work to research, develop and commercialize compounds with activity against an undisclosed metabolic disease target. Janssen granted us an exclusive, worldwide license (with rights to sublicense) under the Janssen know-how and patents to research, develop, make, have made, import, use, offer for sale and sell such compounds. We have full control and responsibility over the research, development and registration of any products developed and/or discovered from the metabolic disease target and are required to use diligent efforts to conduct all such activities.

Abingworth: On July 30, 2021, we entered into a Development Financing Agreement (the Financing Agreement) with ABW Cyclops SPV LP, an affiliate of Abingworth LLP (Abingworth), pursuant to which Abingworth provided us with $75 million of funding to support our development of seladelpar for the treatment of PBC. We have an option to receive an additional $25 million (Optional Funding) within approximately two months of the completion of enrollment of our Phase 3 RESPONSE clinical trial. The Optional Funding is subject to certain customary funding conditions. In return, we will pay to Abingworth (1) contingent upon the first to occur of regulatory approval of seladelpar for the treatment of PBC in the U.S., U.K., Germany, Spain, Italy or France (Regulatory Approval), fixed success payments equal to 2.0x of the funding provided, consisting of $10 million payable within 90 days after Regulatory Approval and thereafter payments due on the first six anniversaries of the Regulatory Approval in the amounts of $15 million, $22.5 million, $22.5 million, $25 million, $27.5 million and $27.5 million, respectively (or if the Optional Funding is provided, 133% of such payments) and (2) variable success payments equal to 1.1x of the funding provided, consisting of sales milestone

payments of (x) $17.5 million and $27.5 million, respectively (or if the Optional Funding is provided, 133% of such payments) upon first reaching certain cumulative U.S. product sales thresholds, and (y) $37.5 million (or if the Optional Funding is provided, 133% of such payment) upon first reaching a specified U.S. product sales run rate.

Promptly following receipt of Regulatory Approval, we are required to execute and deliver a promissory note to Abingworth to convert the fixed and variable success payments into a note payable. At the time that Abingworth receives, collectively, an aggregate of 3.1x of the funding provided (approximately $232.5 million (or $310 million if the Optional Funding is provided)), our payment obligations under the Financing Agreement will be fully satisfied. We have the option to satisfy our payment obligations to Abingworth upon Regulatory Approval, or a change of control of us, by paying an amount equal to the remaining payments payable to Abingworth subject to a mid-single-digit discount rate. Upon a change of control of us, an acceleration payment of 1.35x of the funding provided is payable, net of payments already made to Abingworth and creditable against future payments to Abingworth.

Pursuant to the Financing Agreement, we are required to use commercially reasonable efforts to develop seladelpar and complete our development program in accordance with the Financing Agreement and an agreed timeline. In addition, an executive review committee was established between Abingworth and us to discuss our development of seladelpar.

Pursuant to the Financing Agreement, we granted Abingworth a security interest in all of our assets (other than intellectual property not related to seladelpar), provided that we are permitted to incur certain indebtedness. The security interest will terminate when we have paid Abingworth 2.0x of the funding provided or upon certain terminations of the Financing Agreement. The Financing Agreement also provides for negative, affirmative and additional covenants, with which we have agreed to comply.

The Financing Agreement also provided that we would raise additional funds in a public or private offering within nine months of the effective date of the Financing Agreement, a condition that was satisfied by the equity financing we completed in November 2021.

The Financing Agreement terminates upon the payment of all payments owing to Abingworth, unless earlier terminated. The Financing Agreement may be earlier terminated by Abingworth if (i) we fail to use commercially reasonable efforts to develop seladelpar as set forth in the Financing Agreement or fail to make required payments (Fundamental Breach), (ii) we suffer a material adverse event, (iii) there is a material adverse patent impact on our intellectual property covering seladelpar, (iv) there are certain irresolvable disagreements within the executive review committee, (v) the security interests of Abingworth are invalidated or terminated other than as set forth in the Financing Agreement or (vi) the RESPONSE clinical trial is completed or terminated and (1) the primary endpoint is not met or (2) Abingworth reasonably determines that the results of the RESPONSE clinical trial do not support regulatory approval. The Financing Agreement may be earlier terminated by us if (i) Abingworth fails to fund as provided in the Financing Agreement, (ii) Abingworth fails to release its security interests as provided in the Financing Agreement or (iii) the RESPONSE clinical trial is completed or terminated and the primary endpoint is not met. The Financing Agreement may be terminated by either party (i) if the other party materially breaches the Financing Agreement (Material Breach), (ii) if seladelpar fails to receive regulatory approval in the U.S., U.K. or E.U., (iii) upon the bankruptcy of the other party, (iv) if a serious safety concern arises in a seladelpar clinical trial or (v) upon a change of control of us.

In certain instances, upon the termination of the Financing Agreement, we will be obligated to pay Abingworth a multiple of the amounts paid to us under the Financing Agreement, including specifically,

(i) 310% of such amounts in the event that Abingworth terminates the Financing Agreement due to (x) a Fundamental Breach, (y) our bankruptcy, or (z) a safety concern resulting from gross negligence on our part or due to a safety concern that was material on the effective date of the Financing Agreement and the material data showing such safety concern was not publicly known, disclosed to Abingworth, or in the diligence room made available to Abingworth,

(ii) 200% of such amounts in the event the Financing Agreement is terminated due to (x) our Material Breach or (y) the security interests of Abingworth being invalidated or terminated other than as set forth in the Financing Agreement, and

(iii) 100% of such amounts in the event of certain irresolvable disagreements within the executive review committee.

In addition, if, following certain terminations, we continue to develop seladelpar for the treatment of PBC and obtain Regulatory Approval, we will make the payments to Abingworth as if the Financing Agreement had not been terminated, less any payments made upon termination. We are not obligated to make any payments to Abingworth under certain instances of technical or regulatory failure of the development program.

Research and Development

We do not currently own or operate research and development facilities. We rely on contract service providers (CSPs) including clinical research organizations, clinical trial sites, central laboratories and other service providers to ensure the proper and timely conduct of our clinical trials. While we have agreements governing their activities, we have limited influence over their actual performance. We have relied and plan to continue to rely upon CSPs to monitor and manage data for our ongoing clinical programs for our product candidates, as well as the execution of nonclinical studies. We control only certain aspects of our CSPs' activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CSPs does not relieve us of our regulatory responsibilities. We also rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us, which could also adversely affect the progress of our research, development and commercialization objectives.

Intellectual Property

We own or co-own approximately 30 United States patents and 210 foreign patents, as well as approximately 10 United States patent applications and 50 foreign and Patent Cooperation Treaty applications that are counterparts to certain United States patents and patent applications. In addition, we license from third parties 11 United States patents and 1 United States patent application and approximately 200 foreign patents and 10 foreign and Patent Cooperation Treaty applications that are counterparts to certain United States patents and patent applications. These patents and patent applications include claims covering various aspects of our product pipeline and research and development strategies, including certain PPARd agonists (including seladelpar), their compositions and uses both alone and in combination with other drugs as well as certain GPR119 agonist compositions.

The seladelpar portfolio consists of approximately 400 issued patents and 75 pending patent applications related to composition and method of use that expire between 2025 and 2038, before accounting for any potential patent term extension or orphan disease exclusivity. Patent and trade secret protection is critical to our business. Our success will depend in large part on our ability to obtain, maintain, defend and enforce patents and other intellectual property, to extend the life of patents covering our product candidates, to preserve trade secrets and proprietary know-how, and to operate without infringing the patents and proprietary rights of third parties.

Manufacturing

We do not currently own or operate manufacturing facilities for the production or testing of seladelpar or other product candidates that we develop, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We presently depend on third party contract manufacturers to obtain all of our required raw materials, active pharmaceutical ingredients (APIs) and finished products for our clinical studies for seladelpar. We also expect to use third party contract manufacturers to obtain our commercial supplies of

seladelpar. We have executed manufacturing agreements for our API and clinical supplies of seladelpar with established manufacturing firms that are responsible for sourcing and obtaining the raw materials necessary for the finished products. The raw materials necessary to manufacture the API for seladelpar are available from more than one source.

Competition

The biopharmaceutical industry is highly competitive and subject to rapid and significant innovation. Although we believe that our development expertise and scientific knowledge provide us with advantages over our competitors, particularly in the therapeutic areas in which we are focused, other biopharmaceutical companies in the industry may be able to develop therapeutics that are able to achieve better results. Our competitors include pharmaceutical companies, biotechnology companies, specialty pharmaceutical companies, universities and other research institutions. Many of our competitors have significantly greater financial, technical and human resources than we have.

We have been developing seladelpar for the treatment of patients with PBC and NASH; competition in these indications is discussed further below.

PBC Competition

Currently, the only FDA-approved treatments for PBC are ursodeoxycholic acid (UCDA), also known as ursodiol, an isomer of chenodeoxycholic acid and the synthetic bile acid analog obeticholic acid (Ocaliva®, Intercept Pharmaceuticals). Ursodiol decreases serum levels of ALP, bilirubin, alanine aminotransferase, aspartate aminotransferase, cholesterol, and immunoglobulin M, all of which are elevated in patients with PBC and can serve as biochemical markers of the disease. In a study that combined data from three controlled trials with a total of 548 patients, ursodiol significantly reduced the likelihood of liver transplantation or death after four years. Ursodiol also delayed the progression of hepatic fibrosis in early-stage PBC, but was not effective in advanced disease. It has been reported that up to 50% of PBC patients fail to respond adequately to ursodiol therapy. Ursodiol is available as a generic, is approved for other indications, and is priced at a discount to typical branded therapies used in rare populations.

Ocaliva was approved by the FDA and European Medicines Agency in 2016 for the treatment of PBC in combination with UDCA in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA. Ocaliva also received orphan designations in the U.S. and the E.U. A Phase 3 study was completed with a primary composite endpoint defined as a responder rate comprised of the percentage of patients with ALP < 1.67 times upper limit of normal with a decrease in ALP of at least 15% and total bilirubin less than or equal to upper limit of normal. This study met its goals and Ocaliva was granted accelerated approval based on meeting this primary composite endpoint.

Although not approved for use in PBC, off-label use of fibrate drugs has been reported, though many fibrates are specifically contraindicated for use in PBC due to potential concerns over acute and long-term safety in this patient population. Nevertheless, off-label use of fibrates is mentioned in several published treatment guidelines. Other therapies, such as colchicine, methotrexate, prednisone and multiple immunosuppressive regimens have been attempted. However, their efficacy is limited or unproven, and they are associated with multiple side-effects impacting tolerance and safety. Liver transplantation improves survival in patients with PBC, and it is the only effective treatment for those with liver failure. Liver transplantation however is problematic because of its costs, the limited availability of donor organs, and by the fact that the disease may recur after an initially successful transplantation. As a result, despite the previously mentioned therapeutic interventions, it is recognized that PBC continues to progress in many patients and additional medical treatment is needed to address this disease.

Elafibranor (Genfit S.A./Ipsen, S.A.) is a mixed PPARa/d agonist in development for patients with PBC. In April 2019, Genfit announced elafibranor had been granted Breakthrough Therapy Designation by the FDA for the treatment of PBC. In December 2018, Genfit announced positive Phase 2 results from a Phase 2 study evaluating the efficacy and safety of elafibranor (80 mg and 120 mg once-daily) in adult patients with PBC who had an inadequate response to UDCA. In September 2020, Genfit announced the commencement of a Phase 3 study of elafibranor in patients with PBC who had an inadequate response or intolerance to UDCA. In December 2021 Genfit announced that it had entered into an exclusive licensing agreement with Ipsen for the development and commercialization of elafibranor. Another potential therapy in clinical development for PBC is the dual PPARa/g agonist saroglitazar (Zydus Cadila). In November 2020, Phase 2 results were presented at the Liver Meeting hosted by the American Association for the Study of Liver Disease. In December 2020, Zydus announced saroglitizar had been granted Fast Track Designation for PBC and in January 2021 it received Orphan Drug Designation for PBC by the FDA. In December 2021, Zydus announced it had initiated a Phase 2(b)/3 study of saroglitazar in patients with PBC. The selective NOX inhibitor setanaxib (Calliditas) has also reported Phase 2 study data for PBC and announced its intention to conduct a Phase 2/3 study in PBC commencing in the second half of 2021. In August 2021 Calliditas announced setanaxib had been granted Fast Track Designation for PBC by the FDA and that setanaxib has previously been granted orphan drug designation for PBC in the U.S. and Europe. In cholestatic pruritus, GSK2330672 (GlaxoSmithKline) is an inhibitor of the Intestinal Bile Acid Transporter (IBAT), which is undergoing evaluation for decreasing symptoms of pruritus, including in PBC.

NASH Competition

There are currently no drugs approved in the U.S. or E.U. for the treatment of NASH. In September 2019, Intercept Pharmaceuticals filed a New Drug Application to the U.S. FDA for obeticholic acid in patients with fibrosis due to NASH. Several clinical studies have been completed or are underway with drug candidates that may affect disease outcomes in patients with non-cirrhotic NASH, including Phase 3 studies with OCA, an FXR-agonist (Intercept Pharmaceuticals), cenicriviroc, a CCR2/5 receptor antagonist (Abbvie), and Resmitiron, a THR-beta agonist (Madrigal). Novo Nordisk also commenced a Phase 3 study in NASH in 2021 with semaglutide, a GLP-1 agonist. In addition, over two dozen other compounds are currently in Phase 2 development in NASH.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of products such as those we are developing. The pharmaceutical drug product candidates that we develop must be approved by the Food and Drug Administration (FDA) before they may be legally marketed in the United States.

United States Pharmaceutical Product Development Process

In the United States, the FDA regulates pharmaceutical products under the Federal Food, Drug and Cosmetic Act, and implements regulations. Pharmaceutical products 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 pharmaceutical product 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 Practices (GLP) or other applicable regulations;
- Submission to the FDA of an Investigational New Drug (IND) application, which must become effective before human clinical studies may begin;
- Performance of adequate and well-controlled human clinical studies according to the FDA's current Good Clinical Practices (GCP), to establish the safety and efficacy of the proposed pharmaceutical product for its intended use;
- Submission to the FDA of a New Drug Application (NDA) for a new pharmaceutical product;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the pharmaceutical product is produced to assess compliance with the FDA's current Good Manufacturing Practice standards (cGMP), to assure that the facilities, methods and controls are adequate to preserve the pharmaceutical product's identity, strength, quality and purity;
- Potential FDA audit of selected preclinical and clinical study 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 and the continuing need for compliance with applicable statutes and regulations require the expenditure of substantial resources and approvals are inherently uncertain.

Before testing any compounds with potential therapeutic value in humans, the pharmaceutical 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 pharmaceutical product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLP. 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 has concerns and notifies the sponsor by way of a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical study can begin. The FDA may also impose clinical holds on a pharmaceutical product candidate at any time before or during clinical studies due to safety concerns or non-compliance. Submission of an IND may not result in the FDA allowing clinical studies to begin and, once begun, issues may arise that lead to suspension or termination of such clinical study.

Clinical studies involve the administration of the drug candidate to healthy volunteers or patients under the supervision of qualified investigators, who are generally physicians not employed by or under the clinical study sponsor's control. Clinical studies are conducted under protocols detailing, among other things, the objectives of the clinical study, dosing procedures, subject selection and exclusion criteria, how the results will be analyzed and presented and the parameters to be used to monitor subject safety. Each protocol must be submitted to the FDA as part of the IND. Clinical studies must be conducted in accordance with GCP. Further, each clinical study must be reviewed and approved by an independent Institutional Review Board (IRB) at, or servicing, each institution at which the clinical study will be conducted. An IRB is charged with protecting the welfare and rights of study participants and considers such items as whether the risks to individuals participating in the clinical studies 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 study subject or his or her legal representative and must monitor the clinical study until completed.

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

- Phase 1. The pharmaceutical product is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion.

- Phase 2. The pharmaceutical product 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, to determine dosage tolerance, optimal dosage and dosing schedule and to identify patient populations with specific characteristics where the pharmaceutical product may be more effective.
- Phase 3. Clinical studies are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These clinical studies are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling. The studies must be well-controlled and usually include a control arm for comparison. One or two Phase 3 studies are required by the FDA for an NDA approval, depending on the disease severity and other available treatment options.
- Post-approval studies, or Phase 4 clinical studies, 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.

Progress reports detailing the results of the clinical studies must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events or any finding from tests in laboratory animals that suggests a significant risk for human subjects. Phase 1, Phase 2 and Phase 3 clinical studies 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 study at any time on various grounds, including, but not limited to, a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical study at its institution if the clinical study is not being conducted in accordance with the IRB's requirements or if the drug candidate has been associated with unexpected serious harm to patients.

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

United States Review and Approval Processes

Pre-Approval Requirements

The results of product development, preclinical studies and clinical studies, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the pharmaceutical product, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances.

In addition, under the Pediatric Research Equity Act (PREA), an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the pharmaceutical product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any pharmaceutical product for an indication for which orphan designation has been granted.

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 (PDUFA), the FDA has 10 months from filing in which to complete its initial review of a standard NDA and respond to the applicant, and six months from filing for a priority NDA. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs. The review process and the PDUFA goal date may be extended by three months if the FDA requests or if the NDA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

After the NDA submission is accepted for filing, the FDA reviews the NDA application 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. The FDA may refer applications for novel pharmaceutical products or pharmaceutical products which 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 pharmaceutical product approval process, the FDA also will determine whether a risk evaluation and mitigation strategy (REMS) is necessary to assure the safe use of the pharmaceutical product. 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 manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. If the FDA determines 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. In addition, the FDA will require the review and approval of product labeling.

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 studies are not always conclusive and the FDA may interpret data differently than we interpret the same data. The FDA will issue a complete response letter if the agency decides not to approve the NDA. The complete response letter describes 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 studies. 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 significantly 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 studies designed to further assess pharmaceutical product 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 offers a number of expedited development and review programs for qualifying product candidates. A product intended to treat a serious or life-threatening disease or condition may be eligible for breakthrough

therapy designation to expedite its development and review. A product can receive breakthrough therapy designation if preliminary clinical evidence indicates that the product, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation provides opportunities for frequent interactions with the review team during product development and, once an NDA is submitted, the product may be eligible for priority review. The NDA may also be eligible for rolling review, where the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted.

EMA's recently established PRIME regulatory initiative similarly provides early enhanced regulatory support to facilitate regulatory applications and accelerate the review of medicines that address a high unmet need.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. The orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review or approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusive approval (or exclusivity), which means that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application fee.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective. A comparable orphan drug program is provided under EU law.

Post-Approval Requirements

Any pharmaceutical products for which we receive FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, prohibitions on promoting pharmaceutical products for uses or in patient populations that are not described in the pharmaceutical product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities and promotional activities involving the internet. Failure to comply with FDA requirements can have negative consequences, including adverse publicity, enforcement letters from the FDA, actions by the United States Department of Justice and/or United States Department of Health and Human

Services (HHS) Office of Inspector General, mandated corrective advertising or communications with doctors, and civil or criminal penalties. Although physicians may prescribe legally available pharmaceutical products for off-label uses, manufacturers may not directly or indirectly market or promote such off-label uses.

Manufacturers of our products are required to comply with applicable FDA manufacturing requirements contained in the FDA's cGMP regulations. cGMP regulations require, among other things, quality control and quality assurance, as well as the corresponding maintenance of records and documentation. Pharmaceutical product manufacturers and other entities involved in the manufacture and distribution of approved pharmaceutical products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP 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 restrictions on a product, manufacturer or holder of an approved NDA, including withdrawal of the product from the market. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented and 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, risk minimization action plans and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product.

U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act, or FCPA, prohibits certain individuals and entities, including us, from promising, paying, offering to pay, or authorizing the payment of anything of value to any foreign government official, directly or indirectly, to obtain or retain business or an improper advantage. The U.S. Department of Justice and the U.S. Securities and Exchange Commission, or SEC, have increased their enforcement efforts with respect to the FCPA. Violations of the FCPA may result in large civil and criminal penalties and could result in an adverse effect on a company's reputation, operations, and financial condition. A company may also face collateral consequences such as debarment and the loss of export privileges.

Federal and State HealthCare Laws

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal healthcare laws have been applied to restrict certain business practices in the biopharmaceutical industry in recent years. These laws include anti-kickback statutes, false claims statutes, data privacy and security laws, as well as transparency laws regarding payments or other items of value provided to healthcare providers. The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration to induce or in return for purchasing, leasing, ordering, or arranging for the purchase, lease, or order of any healthcare item or service reimbursable under Medicare, Medicaid, or other federally financed healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payment, ownership interests and providing anything at less than its fair market value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and our practices may not in all cases meet all of the criteria for statutory exemptions or safe harbor protection. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated. The intent standard of the Anti-Kickback Statute was

also broadened by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the PPACA, so that a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below).

The federal False Claims Act prohibits any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus non-reimbursable, uses. Additionally, the civil monetary penalties statute imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payers and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

The federal Physician Payments Sunshine Act, created under the PPACA, and its implementing regulations, require certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually information related to certain payments or other transfers of value provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physicians assistants and nurse practitioners), and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals, and applicable manufacturers and group purchasing organizations to report annually certain ownership and investment interests held by physicians and their immediate family members.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, imposes certain requirements on covered entities, including certain healthcare providers, health plans, and healthcare clearinghouses, and their respective business associates that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity as well as their covered subcontractors relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates". HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

The majority of states also have statutes or regulations similar to the aforementioned federal fraud and abuse laws, some of which are broader in scope and apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Further, 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 or other transfers of value provided to physicians and

other health care providers and entities, marketing expenditures, and drug pricing. Certain state and local laws also require the registration of pharmaceutical sales representatives.

These federal and state laws may impact, among other things, our proposed sales, marketing and education programs. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to significant penalties, including administrative, criminal and civil monetary penalties, damages, fines, imprisonment, exclusion from participation in government healthcare programs, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate its business and our results of operations. To the extent that any of our product candidates are ultimately sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of the FDA approval of the use of our pharmaceutical product candidates, some of our 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 product development and 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 pharmaceutical product is eligible for the extension and the application for the extension must be submitted 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 upon the expected length of the clinical studies and other factors involved in the filing of the relevant NDA.

Market exclusivity provisions under the U.S. Food, Drug, and Cosmetic Act can also delay the submission or the approval of certain applications of other companies seeking to reference another company's NDA. Currently seven years of reference product exclusivity are available to pharmaceutical products designated as orphan drugs, during which the FDA may not approve generic products relying upon the reference product's data. Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric clinical study in accordance with an FDA-issued "Written Request" for such a clinical study.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical 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 upon the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government payors such as Medicare and Medicaid, managed care providers, private health insurers and other organizations. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. While commercial payors often follow Medicare coverage policy and payment limitations, coverage and reimbursement for products can differ significantly from payor to payor. The process for determining whether a payor will provide coverage for a pharmaceutical product may be separate from the

process for setting the price or reimbursement rate that the payor will pay for the pharmaceutical product. Third-party payors may limit coverage to specific pharmaceutical products on an approved list, or formulary, which might not include all of the FDA-approved pharmaceutical 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 in order to demonstrate the medical necessity and cost-effectiveness of its products, in addition to the costs required to obtain the FDA approvals. Our pharmaceutical product candidates may not be considered medically necessary or cost-effective. A payor's decision to provide coverage for a pharmaceutical 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 addition, in the United States there is a growing emphasis on comparative effectiveness research, both by private payors and by government agencies. To the extent other drugs or therapies are found to be more effective than our products, payors may elect to cover such therapies in lieu of our products and/or reimburse our products at a lower rate.

Different pricing and reimbursement schemes exist in other countries. The downward pressure on health care 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 pharmaceutical product candidates for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and we expect this will continue to increase the pressure on pharmaceutical 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.

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the United States federal and state levels that seek to reduce healthcare costs. For example, in March 2010 the PPACA was enacted, which includes measures to significantly change the way healthcare is financed by both governmental and private insurers. Among the provisions of the PPACA of importance to the pharmaceutical and biotechnology industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts to 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;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing manufacturers' Medicaid rebate liability;

- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new transparency reporting requirements under the federal Physician Payments Sunshine Act, created under Section 6002 of the PPACA;
- a requirement to annually report drug samples that manufacturers and distributors provide to physicians;
- expansion of health care fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- a licensure framework for follow-on biologic products;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of a Center for Medicare & Medicaid Innovation at the Centers for Medicare & Medicaid Services (CMS) to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment there have been executive, judicial and Congressional challenges to certain aspects of the PPACA. For example, President Trump signed several Executive Orders and other directives designed to delay the implementation of certain provisions of the PPACA or otherwise circumvent some of the requirements for health insurance mandated by the PPACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the PPACA. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the PPACA and it is unclear how these laws and other efforts to repeal and replace the PPACA will impact the PPACA. On June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the Affordable Care Act will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the PPACA marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the PPACA. It is unclear how any such challenges, and the healthcare reform measures of the Biden administration will impact the PPACA and our business.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. In August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction, or joint committee, to recommend proposals in spending reductions to Congress. The joint committee did not achieve its targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering automatic reductions to several government programs. These reductions include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013 and, due to subsequent legislative amendments, will remain in effect through 2031 unless additional congressional action is taken. However, COVID-19 relief legislation suspended the 2% Medicare sequester from May 1, 2020 through March 31, 2022. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% in the final fiscal year of this sequester. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

More recently, there have been several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that attempt to implement several of the administration's proposals. The FDA also released a final rule and guidance in September 2020, effective November 30, 2020, implementing a portion of the importation executive order providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed pending review by the Biden administration until January 1, 2023. On November 20, 2020, CMS issued an interim final rule implementing President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries. As a result of litigation challenging the Most Favored Nation model, on December 27, 2021, CMS published a final rule that rescinded the Most Favored Nation model interim final rule. In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue to advance these principles. No legislation or administrative actions have been finalized to implement these principles. In addition, Congress is considering drug pricing as part of other reform initiatives. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our business. Further, it is possible that additional governmental action will be taken in response to the COVID-19 pandemic.

International Regulation

In addition to regulations in the United States, there are a variety of foreign regulations governing clinical studies and commercial sales and distribution of our future product candidates. Whether or not FDA approval is obtained for a product, approval of a product must be obtained by the comparable regulatory authorities of foreign countries before clinical studies or marketing of the product can commence in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical studies, product licensing, pricing and reimbursement vary greatly from country to country. In addition, certain regulatory authorities in select countries may require us to repeat previously conducted preclinical and/or clinical studies under specific criteria for approval in their respective country which may delay and/or greatly increase the cost of approval in certain markets targeted for approval by us.

Environment, Health and Safety

Various laws and regulations have been implemented or are under consideration to mitigate the effects of climate change caused by greenhouse gas emissions. For example, the California Air Resources Board is in the process of drafting regulations to meet state emissions targets. Based on current information and subject to the

finalization of the proposed regulations, we believe that our primary risk related to climate change is the risk of increased energy costs. However, because we are not an energy-intensive business, we do not anticipate being subject to a cap and trade system or any other mitigation measures that would likely be material to our capital expenditures, results of operations or competitive position.

We are also subject to other federal, state and local regulations regarding workplace safety and protection of the environment. We use hazardous materials, chemicals, and various compounds in our research and development activities and cannot eliminate the risk of accidental contamination or injury from these materials. Certain misuse or accidents involving these materials could lead to significant litigation, fines and penalties. We have implemented proactive programs to reduce and minimize the risk of hazardous materials incidents.

Corporate Information

CymaBay Therapeutics, Inc., formerly Metabolex, Inc., was incorporated under the laws of the State of Delaware on October 5, 1988, originally under the name Transtech Corporation. Our executive offices are located at 7575 Gateway Blvd., Suite 110, Newark, CA 94560. The telephone number at our executive office is (510) 293-8800. Our corporate website address is www.cymabay.com. We do not incorporate the information contained on, or accessible through, our website into this Annual Report on Form 10-K, and you should not consider it part of this Annual Report. We make available free of charge on or through our website our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act of 1934, as amended, or the Exchange Act, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

Employees

As of December 31, 2021, and February 28, 2022, we had 59 and 60 full-time employees, respectively.

Information about our Executive Officers

As of February 28, 2022, our executive officers were as follows:

Name	Age	Position Held With CymaBay
Sujal Shah	48	President & Chief Executive Officer
Charles A. McWherter, Ph.D.	67	Chief Scientific Officer
Dennis Kim, M.D.	52	Chief Medical Officer
Lewis Stuart	62	Chief Commercial Officer
Klara Dickinson	55	Chief Regulatory and Quality Assurance Officer
Paul T. Quinlan	59	General Counsel and Chief Compliance Officer
Daniel Menold	52	Vice President, Finance

Biographical Information

Sujal Shah has served as our President and Chief Executive Officer since November 2017. Prior to that he served as our Interim President and Chief Executive Officer from March 2017 to November 2017. From December 2013 to March 2017, Mr. Shah served as Chief Financial Officer. Prior to that he served as a consultant and acting Chief Financial Officer for us from June 2012 to December 2013. From 2010 to 2012, Mr. Shah served as Director, Health Care Investment Banking for Citigroup Inc., where he was responsible for managing client relationships and executing strategic and financing related transactions for clients focused in life sciences. From 2004 to 2010 Mr. Shah was employed with Credit-Suisse, last serving in the capacity as Vice President, Health Care Investment Banking Group. Mr. Shah currently serves on the Board of Directors of Tvardi Therapeutics, Inc. and the Executive Advisory Board of the Chemistry of Life Processes Institute at Northwestern University. Mr. Shah received an M.B.A. from Carnegie Mellon University—Tepper School of Business and M.S. and B.S. degrees in Biomedical Engineering from Northwestern University.

Charles A. McWherter, Ph.D. has served as our Chief Scientific Officer since 2013. From 2007 to 2013, he served as our Senior Vice President, Research and Preclinical Development. From 2003 to 2007, he served as Vice President and head of the cardiovascular therapeutics areas of Pfizer Inc., a biopharmaceutical company. From 2001 to 2003, Dr. McWherter served as Vice President of Drug Discovery at Sugen, Inc., a biopharmaceutical company acquired by Pfizer Inc. in 2003. Dr. McWherter obtained his Ph.D. from Cornell University.

Dennis Kim, M.D. has served as our Chief Medical Officer since May 2021. From November 2020 to March 2021 he served as Chief Medical Officer of Afyx Therapeutics, a topical drug delivery company, where he led clinical, medical and regulatory development for Rivelin, a novel mucoadhesive patch to deliver treatment for diseases such as oral lichen planus. Prior to this, from March 2019 to November 2020 he served as Chief Medical Officer of Emerald Health Sciences, a biotechnology company, where he was responsible for the general supervision of the company's clinical and medical affairs, and from September 2011 to February 2019 was Chief Medical Officer at Zafgen, Inc., a biotechnology company, where he was responsible for the general supervision of the company's clinical and medical affairs. Prior to this Dr. Kim served in senior leadership roles at Orexigen, EnteroMedics and Amylin Pharmaceutical. He received his medical degree from The Chicago School of Medicine, completed his internal medicine residency at Rush University Medical College, and specialty fellowship training in endocrinology/metabolism at University of California, San Diego (UCSD) Medical Center. He also holds a M.B.A. with emphasis in biotechnology structure and strategy from UCSD Rady School of Business.

Lewis Stuart has served as our Chief Commercial Officer since May 2021. From December 2019 to May 2021, Mr. Stuart served as Vice President and Prostate Cancer Franchise Leader for Myovant Sciences, a biopharmaceutical company. In this role he led the company's Prostate Cancer Launch Readiness cross functional team of commercial, medical, legal, and manufacturing functions. From 2013 to 2017, Mr. Stuart served as Vice President, US Oncology Franchise at Genomic Health, a healthcare company, in which role he was responsible for various commercial aspects of the company's oncology business. Prior to Genomic Health, Mr. Stuart held senior leadership roles at several leading biopharmaceutical companies including Genomic Health and CV Therapeutics. He received a B.A. in Communications and Marketing Management from Virginia Polytechnic & State University, with graduate studies at Northeastern University.

Klara Dickinson has served as our Chief Regulatory and Quality Assurance Officer since October 2020. Prior to that she was our Chief Regulatory and Compliance Officer since January 2019, and our Senior Vice President, Regulatory Affairs and Compliance since June 2017. Previously, she served as Senior Vice President, Chief Regulatory Officer of Anthera Pharmaceuticals, Inc., a biopharmaceutical company. From 2007 to 2014, she was Senior Vice President of Regulatory Affairs and Compliance at Hyperion Therapeutics Inc, where she was responsible for the general supervision of the company's regulatory affairs and quality assurance. Ms. Dickinson also spent three years at CoTherix, Inc. as Vice President, Regulatory Affairs and Healthcare Compliance Officer, and held various positions at biopharmaceutical companies such as Scios, Inc. and DEY Laboratories (a subsidiary of Mylan, Inc.). Ms. Dickinson holds a B.S. in Biology from the College of Great Falls in Montana and is certified by the Regulatory Affairs Certification Board.

Paul T. Quinlan has served as our General Counsel, Chief Compliance Officer and Corporate Secretary since October 2020. He was also our General Counsel and Corporate Secretary from December 2017 to February 2020. Previously, Mr. Quinlan served as General Counsel and Secretary at TerraVia Holdings, Inc. (formerly Solazyme, Inc.), a biotechnology company, from 2010 until January 2018, where he was responsible for the general supervision of the company's legal affairs. From 2005 to 2010, Mr. Quinlan was General Counsel and Secretary at Metabolex, Inc., a biopharmaceutical company, and from 2000 to 2005, Mr. Quinlan held various positions in the legal department at Maxygen, Inc., a biopharmaceutical company, most recently that of Chief Corporate Securities Counsel. Prior to joining Maxygen, Mr. Quinlan was an associate at Cooley LLP and Cravath, Swaine & Moore LLP. Mr. Quinlan obtained a law degree from Columbia University Law School and a M.Sc. in Medical Biophysics from the University of Toronto.

Daniel Menold has served as our Vice President, Finance since April 2017, and previously served as our Corporate Controller since January 2014. Prior to joining CymaBay, Mr. Menold served as Corporate Controller for technology firm Zoosk, Inc., from 2011 to 2013, where he was responsible for the accounting and financial reporting functions and as Controller and Director of Accounting at Affymetrix, Inc. from 2005 to 2010. Prior to 2005, he also held accounting and finance positions of increasing responsibility at public and private life sciences and high technology companies in the Silicon Valley. Earlier in his career, Mr. Menold was at Ernst & Young LLP where he was an audit manager and served on audits of life sciences and high technology companies. Mr. Menold received a M.S. in accounting and B.S. in finance from The University of Virginia McIntire School of Commerce.

Item 1A. Risk Factors

In addition to the factors discussed elsewhere in this report, the following are important factors that could cause actual results or events to differ materially from those contained in any forward-looking statements made by us or on our behalf. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not currently known to us or that we deem immaterial also may impair our business operations. If any of the following risks or such other risks actually occur, our business could be harmed.

Risks Related to the COVID-19 Pandemic

Our business may be adversely affected by the ongoing COVID-19 pandemic.

While the COVID-19 pandemic did not materially adversely affect our business operations in the years ended December 31, 2021 and 2020, economic and health conditions in the United States and across most of the globe have continued to change during 2021 and thereafter. The emergence of COVID-19 variants, such as the Delta and Omicron variants, have further disrupted the global economy. As a result of the COVID-19 pandemic, including the emergence of new variants, we have experienced and may continue to experience disruptions that could impact aspects of our business, including our progress towards the completion of our clinical studies and other associated drug development activities. Possible future disruptions are currently difficult to foresee and include, but are not limited to, potential risk areas as noted below:

- We are currently managing clinical trials in geographies that are affected by the COVID-19 pandemic, in particular in areas that have been impacted by the emergence of COVID-19 variants such as the Delta and Omicron variants. While we have not experienced material impacts to our clinical activities through December 31, 2021, we are observing impacts due to COVID-19, including reluctance of subjects to enroll in clinical studies due to the ongoing pandemic, travel restrictions impacting trial enrollment, personnel shortages at clinical sites impacting trial enrollment and operations and facility restrictions impacting trial enrollment. We believe that the COVID-19 pandemic, including the emergence of COVID-19 variants, will have a continuing impact on various aspects of our clinical activities in the future. For example, pandemic-related reluctance or restrictions, including stay-at-home orders and curtailment of activities, could reduce the rate of patient enrollment in our RESPONSE clinical trial and other clinical studies, and impair the ability to efficiently treat patients at investigator sites. Additionally, our employees, representatives from our clinical research organization partners, and study investigators may be unable to efficiently collaborate or unwilling to conduct investigator site activities in-person at the sites (as per standard practice) and may be required to delay, or alter, their approach to complete this work due to shortages of personnel or diversion of resources at clinical sites or continued government-imposed limitations on activities. Further, our employees and representatives from our contract manufacturing organizations may experience unanticipated challenges sourcing raw materials or producing and distributing sufficient quantities of clinical drug supplies for use in our clinical trials.
- We have limited access to our corporate office and most of our personnel, including all of our administrative employees, work remotely. We have restricted on-site staff to only those personnel and contractors who must perform essential activities that must be completed on-site. The COVID-19

pandemic could disrupt our ability to secure supplies for our operations. The safety, health and well-being of our workforce is of primary concern and we may need to enact further precautionary measures to help minimize the risk of our employees being exposed to the coronavirus.

- Our increased and continuing reliance on personnel working from home may negatively impact productivity, or disrupt, delay, or otherwise adversely impact our business. In addition, this could increase our cyber-security and data privacy risks, create data accessibility concerns, and make us more susceptible to communication disruptions, any of which could adversely impact our business operations, or delay necessary interactions with regulators, contract manufacturers, contract research organizations, clinical trial sites, and other important agencies and contractors, which could result in increased costs to us.
- Our employees and contractors involved in conducting our research and development activities may not be able to access their applicable work facilities for an extended period of time as a result of facility closure orders and the possibility that governmental authorities further modify such access restrictions.
- The United States Food and Drug Administration (FDA), comparable foreign regulatory agencies, and ethics boards may experience operational interruptions or delays, which could impact timelines for regulatory meetings, submissions, trial initiations, and regulatory approvals.

The COVID-19 pandemic continues to evolve. The emergence of COVID-19 variants, such as the Delta and Omicron variants, will also continue to affect the impact of the pandemic. The extent to which the pandemic may impact our business, including our preclinical, clinical and associated drug development activities, will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of COVID-19, variants to COVID-19 that continue to arise and their relative transmissibility and virulen, the duration of the pandemic, travel restrictions and actions to contain the pandemic or treat its impact, such as social distancing and quarantines or lock-downs in the United States, particularly in the San Francisco Bay Area where our executive offices are located, and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

Risks Related to Our Financial Condition and Capital Requirements

We will need additional capital in the future to sufficiently fund our operations and research.

We have incurred significant net losses since our inception. We anticipate that we will continue to incur significant losses for the foreseeable future, and we may never achieve or maintain profitability. As of December 31, 2021, we had cash, cash equivalents and marketable securities of approximately $194.6 million. On July 30, 2021, we entered into a Development Financing Agreement with an affiliate of Abingworth LLP pursuant to which Abingworth has committed to provide us up to $100.0 million in funding, of which we have already received $75 million. In November 2021, we sold 15,625,000 shares of common stock at $4.00 per share and pre-funded warrants to purchase 3,125,000 shares of common stock at $3.9999 per share in a public equity offering, for total gross offering proceeds of approximately $75 million, before deducting the underwriting fees and other offering expenses. We may need to raise additional equity and/or debt capital to fund our continued operations, including clinical trials and other product development. We may also choose to raise additional equity and/or debt capital if appropriate opportunities become available. Our monthly spending levels vary based on new and ongoing development and corporate activities. Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a time-consuming, expensive and uncertain process that takes years to complete.

In the event we do not successfully raise sufficient funds to finance our product development activities, we will curtail our product development activities commensurate with the magnitude of the shortfall or our product development activities may cease altogether. To the extent that the costs of ongoing development exceed our current estimates and we are unable to raise sufficient additional capital to cover such additional costs, we will

need to reduce operating expenses, sell assets, enter into strategic transactions, or effect a combination of the above. No assurance can be given that we will be able to enter into any of such transactions on acceptable terms, if at all.

Our future funding requirements and sources will depend on many factors, including but not limited to the following:

- the rate of progress and cost of our clinical studies;
- the need for additional or expanded clinical studies;
- the rate of progress and cost of our Chemistry, Manufacturing and Control development, registration, validation and commercial programs;
- the timing, economic and other terms of any licensing, collaboration or other similar arrangement into which we may enter;
- the costs and timing of seeking and obtaining FDA and other regulatory approvals;
- the extent of our other development activities;
- the costs of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights; and
- the effect of competing products and market developments.

If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we will be prevented from pursuing development and commercialization efforts, which would have a material adverse effect on our business, operating results, prospects, and on our ability to develop our product candidates.

Failure to remain in compliance with our obligations under the development financing agreement with Abingworth could lead to reduced funding under the agreement and/or the acceleration of potentially significant payments to Abingworth.

On July 30, 2021, we entered into a Development Financing Agreement (the Financing Agreement) with Abingworth, pursuant to which Abingworth agreed to provide funding to us to support our development of seladelpar for the treatment of PBC. Pursuant to the Financing Agreement, Abingworth has committed to provide us up to $100.0 million in funding, of which we have received $75 million through March 2022. Pursuant to the Financing Agreement, we will be required to use commercially reasonable efforts to develop seladelpar and complete our development program in accordance with the Financing Agreement and an agreed timeline. In return, we will pay to Abingworth (1) upon the first to occur of regulatory approval of seladelpar for the treatment of PBC in the U.S., U.K., Germany, Spain, Italy or France (Regulatory Approval), fixed success payments equal to 2.0x of the funding provided and (2) variable success payments equal to 1.1x of the funding provided upon first reaching certain U.S. product sales milestones. At the time that Abingworth receives, collectively, an aggregate of 3.1x of the funding provided, our payment obligations under the Financing Agreement will be fully satisfied.

The Financing Agreement terminates upon the payment of all payments owing to Abingworth, unless earlier terminated. The Agreement may be earlier terminated in a number of circumstances including (i) by Abingworth if we fail to use commercially reasonable efforts to develop seladelpar as set forth in the Financing Agreement or if we fail to make required payments (Fundamental Breach) or (ii) by either party if the other party materially breaches the Agreement (Material Breach). In certain instances, upon the termination of the Financing Agreement, we will be obligated to pay Abingworth a multiple of the amounts paid to us under the Agreement, including specifically,

(i) 310% of such amounts in the event that Abingworth terminates the agreement due to (x) a Fundamental Breach, (y) our bankruptcy, or (z) a safety concern resulting from gross negligence on our part or due to a safety concern that was material on the Effective Date and the material data showing such safety concern was not publicly known, disclosed to Abingworth, or in the diligence room made available to Abingworth,

(ii) 200% of such amounts in the event the Agreement is terminated due to (x) our Material Breach or (y) the security interests of Abingworth being invalidated or terminated other than as set forth in the Financing Agreement, and

(iii) 100% of such amounts in the event of certain irresolvable disagreements within the executive review committee overseeing our development of seladelpar.

In addition, if, following certain terminations, we continue to develop seladelpar for the treatment of PBC and obtain Regulatory Approval, we will make the payments to Abingworth as if the Financing Agreement had not been terminated, less any payments made upon termination.

The payments required under the Financing Agreement are significant. Failure to generate sufficient revenue to make such payments if and as they become due, or failure to otherwise finance such payments would have a material adverse effect on our business. In addition, if we are unable to comply with our obligations under the Financing Agreement and/or one of the termination events described above occurs, Abingworth may be relieved of their obligation to provide further funding under the Financing Agreement and our payments obligations thereunder may be accelerated. The acceleration of payments under the Financing Agreement would have a material impact on our business and we may not be able to make such payments at such time.

Our ability to generate future revenues from product sales is uncertain and depends upon our ability to successfully develop, obtain regulatory approval for, and commercialize product candidates.

Our ability to generate revenue and achieve profitability depends on our ability, alone or with collaborators, to successfully complete the development of, obtain the necessary regulatory approvals for, and commercialize, product candidates. We do not anticipate generating revenues from sales of our product candidates in the near future, if ever.

Conducting preclinical testing and clinical trials is a time-consuming, expensive, and uncertain process that takes years to complete, and we may never generate the necessary data required to obtain regulatory approval and achieve product sales. Our anticipated development costs would likely increase if we do not obtain favorable results or if development of our product candidates is delayed. In particular, we would likely incur higher costs than we currently anticipate if development of our product candidates is delayed because we are required by a regulatory authority such as the FDA to perform studies or trials in addition to those that we currently anticipate. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to predict the timing or amount of any increase in our anticipated development costs.

In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for several years, if at all. Even if one or more of our product candidates is approved for commercial sale, we anticipate incurring significant costs in connection with commercialization. As a result, we cannot assure you that we will be able to generate revenues from sales of any approved products, or that we will achieve or maintain profitability even if we do generate sales.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing and distribution arrangements. We do not have any committed external source of funds other than the Financing Agreement. If appropriate opportunities become available, we may seek to raise additional equity and/or debt capital to fund our continued operations, including clinical trials and other product development.

To raise additional funds to support our operations, we may sell additional equity or debt securities, enter into collaborations, strategic alliances, or licensing arrangements or other marketing or distribution arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, ownership

interests of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, and declaring dividends, and may impose limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business.

If we raise additional funds through collaborations, strategic alliances, or licensing arrangements or other marketing or distribution arrangements with third parties, we may have to relinquish valuable rights to our intellectual property, technologies, future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us.

If we are unable to expand our operations or otherwise capitalize on our business opportunities, our business, financial condition and results of operations could be materially adversely affected. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts, or grant others rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to Clinical Development and Regulatory Approval

We depend on the success of our product candidates and we may not obtain regulatory approval or successfully commercialize our product candidates.

We have not marketed, distributed or sold any products. The success of our business depends upon our ability to develop and commercialize our product candidates. The success of any product candidate will depend on many factors, including the following:

- successful enrollment and completion of clinical trials, including, in the case of RESPONSE, enrollment of sufficient subjects willing to receive a liver biopsy;
- receipt of marketing approvals from the FDA and regulatory authorities outside the United States for the product candidate;
- establishing commercial manufacturing capabilities by making arrangements with third-party manufacturers;
- launching commercial sales of the product, whether alone or in collaboration with others;
- acceptance of the product by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- a continued acceptable safety profile of the product following marketing approval; and
- obtaining, maintaining, enforcing and defending intellectual property rights and claims.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidate, which would materially harm our business.

We depend on the successful completion of clinical trials for our product candidates.

Before obtaining regulatory approval for the sale of our product candidates, we must complete our current clinical trials as well as potentially additional clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more of our clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical

and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for their products.

We may experience a number of unforeseen events during clinical trials for our product candidates, including seladelpar, that could delay or prevent the commencement and/or completion of our clinical trials, including the following:

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- the clinical study protocol may require one or more amendments delaying study completion;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of subjects required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be insufficient or slower than we anticipate, we may have to compete with other clinical trials to enroll eligible subjects, or subjects may drop out of these clinical trials at a higher rate than we anticipate;
- the number of patients in our RESPONSE clinical trial that choose to have biopsies may be insufficient to satisfy regulatory requirements;
- clinical investigators or study subjects may fail to comply with clinical study protocols;
- trial conduct and data analysis errors may occur, including, but not limited to, data entry and/or labeling errors;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we might have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the subjects are being exposed to unacceptable health risks;
- geo-political turmoil between Russia and Ukraine and/or continuing military actions in Ukraine may cause us to have to suspend or terminate clinical trials of seladelpar in those countries;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our clinical trial materials or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators to suspend or terminate the trials.

Because successful development of product candidates is uncertain, we are unable to estimate the actual funds required to complete research and development and commercialize our products under development.

Negative or inconclusive results of our future clinical trials of product candidates could cause the FDA or other regulatory authorities to require that we repeat or conduct additional clinical studies. If later stage clinical trials do not produce favorable results, our ability to obtain regulatory approval for our product candidates may be adversely impacted.

Geo-political turmoil between Russia and Ukraine and continuing military actions in Ukraine have caused us to suspend clinical trial activity in Ukraine and suspend screening in Russia and may, together with widening sanctions imposed on Russia, cause us to suspend or terminate all clinical trial activity in Russia.

We have a small number of clinical sites in both Russia and Ukraine in our RESPONSE clinical trial and in Russia in our ASSURE clinical trial. Because of continuing military action in Ukraine we recently suspended clinical trial activity in Ukraine. This suspension could potentially delay enrollment completion in our RESPONSE trial. Ongoing geo-political turmoil and continuing military action in the region, together with widening sanctions imposed on Russia, have also caused us to suspend screening in Russia and may cause us to need to suspend or terminate all clinical trial activity in Russia. Even if all activity is not suspended or terminated, the ongoing military action and sanctions may affect our RESPONSE and ASSURE clinical trials in Russia. Shipments of seladelpar to Russia may become difficult, delayed or impossible. Shipments of clinical samples from Russia may also become difficult, delayed or impossible. In addition, sites, site personnel and patients may not be able to continue in the trials and we may need to suspend or terminate the trials in Russia. While we have only a small number of clinical sites and enrolled patients in Russia, these disruptions and suspensions could potentially delay enrollment completion in our RESPONSE clinical trial and/or complicate the analysis of data from subjects in Russia.

Delays in clinical trials are common and have many causes, and any delay could result in increased costs to us and jeopardize or delay our ability to obtain regulatory approval and commence product sales.

Clinical testing is expensive, difficult to design and implement, can take many years to complete, and is uncertain as to outcome. We may experience delays in clinical trials at any stage of development and testing of our product candidates and any delay could result in increased costs to us. Any clinical trials we undertake may not begin on time, have an effective design, enroll a sufficient number of subjects, or be completed on schedule, if at all. The impact of the ongoing COVID-19 pandemic, including the emergence of COVID-19 variants such as the Delta and Omicron variants, is also uncertain, and may create additional delays in completing our clinical trials.

Events that may result in delays or unsuccessful completion of clinical trials include the following:

- reluctance of patients to enroll in our clinical trials due to the COVID-19 pandemic;
- personnel shortages at clinical sites due to the COVID-19 pandemic that impact the enrollment timeline or operations at clinical trial sites participating in our clinical trials;
- competition for eligible patients from competing clinical trials;
- delays in obtaining regulatory approval to commence a trial;
- delays in reaching agreement with the FDA or other regulatory authorities on final trial design;
- imposition of a clinical hold following a reported safety event;
- an inspection of our clinical trial operations or trial sites by the FDA or other regulatory authorities;
- delays in reaching agreement on acceptable terms with prospective contract research organizations (CROs) and clinical trial sites;
- delays in obtaining required institutional review board (IRB) approval at each site;
- delays in recruiting suitable patients to participate in a trial;
- delays in having subjects complete participation in a trial or return for post-treatment follow-up;
- delays caused by the need to enroll additional subjects willing to have biopsies in the RESPONSE trial;
- delays caused by subjects dropping out of a trial due to side effects or otherwise;

- changes to treatment guidelines or the introduction of a new standard of care;
- delays caused by clinical sites dropping out of a trial;
- time required to add new clinical sites;
- delays by our contract manufacturers to produce and deliver sufficient supply of clinical trial materials; and
- delays in importing clinical trial materials into foreign countries where our clinical trials are being conducted.

If initiation or completion of any clinical trials we may undertake for our product candidates is delayed for any of the above reasons, our development costs may increase, the approval process could be delayed, any periods during which we may have the exclusive right to commercialize our product candidates may be reduced and our competitors may bring products to market before us. Any of these events could impair our ability to generate revenues from product sales, which would have a material adverse effect on our business.

Our product candidates may cause adverse effects or have other properties that could delay or prevent their regulatory approval or limit the scope of any approved label or market acceptance.

In May 2016, we announced results of a High Dose Phase 2 clinical study of seladelpar in patients with PBC. During the course of this trial three cases of asymptomatic, reversible transaminase elevations occurred, and we made the decision to discontinue the study early after review of safety and efficacy data demonstrated a need for further dose reduction to optimize clinical safety and efficacy. In November and December 2019, due to histologic observations in our NASH clinical trial, all seladelpar clinical trials were terminated, pending further analysis of data from the NASH trial and further discussions with the FDA. Although in July 2020 the FDA lifted the clinical hold on our seladelpar program, this process substantially delayed the development of seladelpar. The emergence of adverse events (AEs) and histological observations in subsequent seladelpar clinical trials could prevent us from further developing seladelpar or could result in the denial of regulatory approval.

Furthermore, if any of our approved products cause serious or unexpected side effects after receiving market approval, a number of potentially significant negative consequences could result, including the following:

- regulatory authorities may withdraw their approval of the product or impose restrictions on its distribution in a form of a risk evaluation and mitigation strategy (REMS) plan;
- regulatory authorities may require the addition of labeling statements, such as black box or other warnings or contraindications that could diminish the usage of the product or otherwise limit the commercial success of the affected product;
- we may be required to change the way the product is administered or to conduct additional clinical studies;
- we may choose to discontinue sale of the product;
- we could be sued and held liable for harm caused to patients; or
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product and could substantially increase the costs of commercializing our product candidates.

Potential conflicts of interest arising from relationships with principal investigators for our clinical studies and any related compensation with respect to clinical studies could adversely affect the drug approval process.

Principal investigators for our clinical studies may serve as scientific advisors or consultants to us or may be affiliated with our other service providers, including clinical research organizations or site management

organizations, and from time to time receive cash compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, the integrity of the data generated at the applicable clinical study site or in the applicable study may be questioned or jeopardized.

We may be subject to costly claims related to our clinical studies and may not be able to obtain adequate insurance.

Because we conduct clinical studies in humans, we face the risk that the use of seladelpar or other product candidates will result in adverse side effects. We cannot predict the possible harms or side effects that may result from our clinical studies. Although we have clinical study liability insurance, our insurance may be insufficient to cover any such events. There is also a risk that we may not be able to continue to obtain clinical study coverage on acceptable terms. In addition, we may not have sufficient resources to pay for any liabilities resulting from a claim excluded from, or beyond the limit of, our insurance coverage. There is also a risk that third parties that we have agreed to indemnify could incur liability. Any litigation arising from our clinical studies, even if we are ultimately successful, would consume substantial amounts of our financial and managerial resources and may create adverse publicity.

After the completion of our clinical trials, we cannot predict whether or when we will obtain regulatory approval to commercialize our product candidates and we cannot, therefore, predict the timing of any future revenue from our product candidates. Regulatory approval of a product candidate is not guaranteed, and the approval process is expensive, uncertain and lengthy.

We cannot commercialize our product candidates until the appropriate regulatory authorities, such as the FDA, have reviewed and approved the product candidate. The regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval for our product candidates. Additional delays may result if a product candidate is brought before an FDA advisory committee, which could recommend restrictions on approval or recommend non-approval of the product candidate. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical studies and the review process. As a result, we cannot predict when, if at all, we will receive any future revenue from commercialization of any of our product candidates. The FDA and foreign regulatory authorities have substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons, including the following:

- we may be unable to demonstrate to the satisfaction of regulatory authorities that a product candidate is safe and effective for any indication;
- regulatory authorities may not find the data from nonclinical studies and clinical studies sufficient or may differ in the interpretation of the data;
- regulatory authorities may require additional nonclinical or clinical studies;
- regulatory authorities might not approve our third party manufacturers' processes or facilities for clinical or commercial product;
- regulatory authorities may change their approval policies or adopt new regulations;
- regulatory authorities may disagree with the design or implementation of our clinical studies;
- regulatory authorities may not accept clinical data from studies that are conducted in countries where the standard of care is potentially different from the jurisdiction of that regulatory authority;
- the results of clinical studies may not meet the level of statistical significance required by regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks; and

- the data collection from clinical studies of our product candidates may not be sufficient to support the submission of a new drug application (NDA), marketing authorization or other equivalent submission, or to obtain regulatory approval in the United States or elsewhere.

In addition, events raising questions about the safety of certain marketed pharmaceuticals may result in increased caution by the FDA and other regulatory authorities in reviewing new pharmaceuticals based on safety, efficacy or other regulatory considerations and may result in significant delays in obtaining regulatory approvals.

Even if we obtain regulatory approval for our product candidates, we will still face extensive regulatory requirements and our products may face future development and regulatory difficulties.

Even if we obtain regulatory approval in the United States, the FDA may still impose significant restrictions on the indicated uses or marketing of our products or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. Our products would be subject to additional ongoing FDA requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, record-keeping and reporting of safety and other post-market information. The holder of an approved NDA is obligated to monitor and report AEs and any failure of a product to meet the specifications in the NDA. The holder of an approved NDA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws. Furthermore, promotional materials must be approved by the FDA prior to use for any drug receiving accelerated approval.

In addition, manufacturers of drug products and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current Good Manufacturing Practices (cGMP), and adherence to commitments made in the NDA. If we, or a regulatory agency, discover previously unknown problems with a product, such as quality issues or AEs of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requesting recall or withdrawal of the product from the market or suspension of manufacturing.

If we, or our third-party contractors, fail to comply with applicable regulatory requirements following approval of our product candidate, a regulatory agency may:

- issue an untitled or warning letter asserting violation of the law;
- seek an injunction or impose civil or criminal penalties up to and including imprisonment or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending NDA or supplements to an NDA; or
- request recall and/or seize product.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our products and inhibit our ability to generate revenues.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products. If we are found to have improperly promoted our products for off-label uses, we may become subject to significant fines and other liability.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we receive marketing approval for our product candidates, physicians may nevertheless prescribe such products to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant government fines and other related liability. For example, the federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA also has requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Even if we obtain FDA approval for our product candidates in the United States, we may never obtain approval for or commercialize our product candidates outside of the United States, which would limit our ability to realize their full market potential.

In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements on a country-by-country basis regarding safety and efficacy. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and costs for us and require additional preclinical studies or clinical trials that could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our products will be unrealized.

Coverage and adequate reimbursement may not be available for our future products, which could make it difficult for us to sell profitably, if approved.

Market acceptance and sales of any products that we commercialize will depend in part on the extent to which coverage and adequate reimbursement will be available from third-party payers, including government health administration authorities, managed care organizations and private health insurers. Third-party payers decide which therapies they will pay for and establish reimbursement levels. Third-party payers in the United States often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. However, decisions regarding the extent of coverage and amount of reimbursement to be provided for any products that we develop will be made on a payer-by-payer basis. One payer's determination to provide coverage for a drug does not assure that other payers will also provide coverage and adequate reimbursement for the drug. Additionally, a third-party payer's decision to provide coverage for a therapy does not imply that an adequate reimbursement rate will be approved. Third-party payers are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. We cannot be sure that coverage and reimbursement in the United States or elsewhere will be available for any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Our relationships with health care professionals, customers and payors may be subject to applicable anti-kickback, fraud and abuse and other health care laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Health care professionals and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, third-party payors and customers may expose us to broadly applicable fraud and abuse and other health care laws and regulations that may constrain the business or financial arrangements and relationships through which we research, as well as market, sell and distribute our products. Restrictions under applicable federal and state health care laws and regulations, include the federal Anti-Kickback Statute, the federal False Claims Act, the Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, the federal false statements statute, the federal transparency requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or PPACA, commonly referred to as the Physician Payments Sunshine Act, and analogous state laws and regulations, such as state anti-kickback and false claims laws.

Efforts to ensure that our business arrangements with third parties will comply with applicable health care 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 health care 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, disgorgement, exclusion from government funded health care programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded health care programs.

Current laws and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the health care system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any products for which we obtain marketing approval.

For example, the PPACA was enacted to broaden access to health insurance, reduce or constrain the growth of health care spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Since its enactment there have been judicial and Congressional challenges to certain aspects of the PPACA as well as efforts to repeal or replace certain aspects of the PPACA. For example, Congress considered legislation that would repeal or repeal and replace all or part of the PPACA. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the PPACA. It is unclear how litigation, and the healthcare reform measures of the Biden administration will impact the PPACA and our business.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. In addition, there have been several recent congressional inquiries, proposed bills and other proposals designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products including instituting reference pricing. At the federal level, the Trump administration used several means to propose or implement drug pricing

reform, including through federal budget proposals, executive orders and policy initiatives. However, it is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We are not sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. Further, it is possible that additional governmental action is taken in response to the COVID-19 pandemic.

Risks Related to Our Reliance on Third Parties

We rely on third-party manufacturers to produce our preclinical and clinical drug supplies, and we intend to rely on third parties to produce commercial supplies of any approved products.

We do not own or operate, and we do not expect to own or operate, facilities for product manufacturing, storage and distribution, or testing. We currently rely on third-party manufacturers for supply of our preclinical and clinical drug supplies. We expect that in the future we will continue to rely on such manufacturers for drug supplies that will be used in clinical trials of our product candidates, and for commercialization of any of our product candidates that receive regulatory approval.

The facilities used by our contract manufacturers to manufacture the approved product must be approved by the FDA pursuant to inspections that will be conducted only after we submit an NDA to the FDA, if at all. A representative from the EMA or another regulatory authority may also require inspection and approval of such contract manufacturing facilities. We are completely dependent on our contract manufacturing partners for compliance with the FDA's requirements for manufacture of finished pharmaceutical products. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the FDA's strict regulatory requirements of safety, purity and potency, we will not be able to secure and/or maintain FDA approval for our product candidates. In addition, we have no direct control over the ability of the contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If our contract manufacturers cannot meet FDA standards, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our products. No assurance can be given that our manufacturers can continue to make clinical and commercial supplies of product candidates, at an appropriate scale and cost to make it commercially feasible.

In addition, we do not have the capability to package and distribute finished products to pharmacies and other customers. If we receive marketing approval from the FDA, we intend to sell pharmaceutical product packaged and distributed by one or more pharmaceutical product packagers/distributors. Although we have entered into agreements with our current contract manufacturers and packager/distributor for clinical trial material, we will need to enter into commercial agreements with contract manufacturers and with one or more pharmaceutical product packagers/distributors to ensure proper supply chain management once we are authorized to make commercial sales of our product candidates. However, we may be unable to maintain agreements or negotiate commercial supply agreements on commercially reasonable terms with contract manufacturers and pharmaceutical product packagers/distributors, which could delay our ability to launch commercial sales and/or have a material adverse impact upon our business.

We rely on limited sources of supply for our product candidates, and any disruption in the chain of supply may cause delay in developing and commercializing for each product candidate.

If supply from an approved vendor is interrupted, there could be a significant disruption in commercial supply of our products. An alternative vendor would need to be qualified through a supplemental registration,

which would be expensive, time consuming and could result in further delay. The FDA or other regulatory agencies outside of the United States may also require additional studies if a new drug substance or drug product supplier is relied upon for commercial production. These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our products, and cause us to incur additional costs. Furthermore, if our suppliers fail to deliver the required commercial quantities of active pharmaceutical ingredient on a timely basis and at commercially reasonable prices, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, the supply chain for our products may be delayed, which could inhibit our ability to generate revenues.

Manufacturing issues may arise that could increase product and regulatory approval costs or delay commercialization of our products.

As the manufacturing processes are scaled up they may reveal manufacturing challenges or previously unknown impurities that could require resolution in order to proceed with our planned clinical trials and obtain regulatory approval for the commercial marketing of our products. In the future, we may identify manufacturing issues or impurities that could result in delays in the clinical program and regulatory approval for our products, increases in our operating expenses, or failure to obtain or maintain approval for our products.

Our reliance on third-party manufacturers entails risks, including the following:

- the inability to meet our product specifications, including product formulation, and quality requirements consistently;
- a delay or inability to procure or expand sufficient manufacturing capacity;
- manufacturing and product quality issues, including those related toscale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;
- a failure to comply with cGMP and similar quality standards;
- the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- the reliance on a limited number of sources, and in some cases, single sources for key materials, such that if we are unable to secure a sufficient supply of these key materials, we will be unable to manufacture and sell our products in a timely fashion, in sufficient quantities or under acceptable terms;
- the lack of qualified backup suppliers for those materials that are currently purchased from a sole or single source supplier;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier;
- disruption of the distribution of chemical supplies between the U.K. and E.U. due to Brexit;
- carrier disruptions or increased costs that are beyond our control; and
- the failure to deliver our products under specified storage conditions and in a timely manner.

Any of these events could lead to delays in any clinical study we may undertake, failure to obtain regulatory approval or impact our ability to successfully commercialize our products. Some of these events could be the basis for FDA or other regulatory authorities' action, including injunction, recall, seizure, or total or partial suspension of production.

We rely on third parties to conduct, supervise and monitor our clinical studies, and if those third parties perform in an unsatisfactory manner, it may harm our business.

We rely on contract service providers (CSPs), including clinical research organizations, clinical trial sites, central laboratories and other service providers to ensure the proper and timely conduct of our clinical trials. While we have agreements governing their activities, we have limited influence over their actual performance. We have relied and plan to continue to rely upon CSPs to monitor and manage data for clinical programs for our product candidates, as well as the execution of nonclinical studies. We control only certain aspects of our CSPs' activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CSPs does not relieve us of our regulatory responsibilities.

We and our CSPs are required to comply with the FDA's guidance, which follows the International Counsel for Harmonization Good Clinical Practice (ICH GCP), which are regulations and guidelines enforced by the FDA for all of our product candidates in clinical development. The FDA enforces the ICH GCP through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CSPs fail to comply with the ICH GCP, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our marketing applications. Our CSPs are not our employees, and we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and nonclinical programs. These CSPs may also have relationships with other entities, including our competitors, for whom they may also be conducting clinical studies, or other drug development activities that could harm our competitive position. We face the risk of potential unauthorized disclosure or misappropriation of our confidential information, including our intellectual property, by CSPs, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology, among other things. If our CSPs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates that we develop would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

Risks Related to Commercialization of Our Product Candidates

The commercial success of any product will depend upon the acceptance of these products by the medical community, including physicians, patients and health care payors.

If any of our product candidates receive marketing approval, they may nonetheless be unable to gain sufficient market acceptance by physicians, patients, health care payors and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of any of our products will depend on a number of factors, including the following:

- demonstration of clinical safety and efficacy in our clinical trials;
- the risk/benefit profile of our products;
- the relative convenience, ease of administration and acceptance by physicians, patients and health care payors;
- the prevalence and severity of any side effects;
- the safety of products seen in a broader patient group, including its use outside the approved indications;

- limitations or warnings contained in the FDA and other regulatory authorities approved label for the relevant product;
- acceptance of the product by physicians, other health care providers and patients as a safe and effective treatment;
- the potential and perceived advantages of products over alternative treatments;
- the timing of market introduction of competitive products;
- pricing and cost-effectiveness;
- the effectiveness of our or any future collaborators' sales and marketing strategies;
- our ability to obtain formulary approval;
- our ability to obtain and maintain sufficient third-party coverage or reimbursement, which may vary from country to country; and
- the effectiveness of our or any future collaborators' sales, marketing and distribution efforts.

If any of our product candidates is approved but does not achieve an adequate level of acceptance by physicians, patients and health care payors, we may not generate sufficient revenue and we may not become or remain profitable.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product, we may be unable to generate any revenue.

We currently do not have an organization for the sales, marketing and distribution of pharmaceutical products and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. In order to market any products that may be approved we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. We may enter into strategic partnerships with third parties to commercialize our products.

If we are unable to build our own sales force or negotiate a strategic partnership for the commercialization of our products, we may be forced to delay the potential commercialization of the product, or reduce the scope of our sales or marketing activities. If we elect to increase our expenditures to fund commercialization activities ourselves, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we will not be able to bring the product to market or generate product revenue.

If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate sufficient product revenue and may not become profitable. We will be competing with companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform sales and marketing functions, we may be unable to compete successfully against these more established companies.

In addition, there are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

If we obtain approval to commercialize any products outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If our product candidates are approved for commercialization outside the United States, we expect that we will be subject to additional risks related to international operations, including the following:

- different regulatory requirements for drug approvals in foreign countries;

- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- differing payor reimbursement regimes, governmental payors or patientself-pay systems and price controls;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, pandemics, or natural disasters including earthquakes, typhoons, volcanic eruptions, floods and fires.

We have no prior experience in these areas. In addition, there are complex regulatory, tax, labor and other legal requirements imposed by both the European Union and many of the individual countries in Europe with which we would need to comply. Many U.S.-based biopharmaceutical companies have found the process of marketing their own products in Europe to be very challenging.

If our competitors develop and market products that are more effective, safer or less expensive than our own, our commercial opportunities will be negatively impacted.

The life sciences industry is highly competitive, and we face significant competition from other pharmaceutical, biopharmaceutical and biotechnology companies and possibly from academic institutions, government agencies and private and public research institutions that are researching, developing and marketing products designed to address diseases that we are seeking to treat. Our competitors generally have significantly greater financial, manufacturing, marketing and drug development resources. Large pharmaceutical companies, in particular, have extensive experience in the clinical testing of, obtaining regulatory approvals for, and marketing of, drugs. New developments, including the development of other pharmaceutical technologies and methods of treating disease, occur in the pharmaceutical and life sciences industries at a rapid pace.

These developments may render our product candidates obsolete or noncompetitive. Compared to us, potential competitors may have substantially greater:

- research and development resources, including personnel and technology;
- regulatory experience;
- experience in pharmaceutical development and commercialization;
- ability to negotiate competitive pricing and reimbursement with third-party payors;
- experience and expertise in the exploitation of intellectual property rights; and
- capital resources.

As a result of these factors, our competitors may obtain regulatory approval of their products more rapidly than we do or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidates. The competitors may also develop products that are more effective, better tolerated, more useful and less costly than our products and they may also be more successful in manufacturing and marketing their products.

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 exposure related to the testing of our product candidates in human clinical studies, and will face an even greater risk if we sell our products commercially. An individual or a group of individuals may bring a liability claim against us if one of our product candidates causes, or merely appears to have caused, an injury. If we cannot successfully defend ourselves against product liability claims, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in the following:

- decreased demand for our products;
- impairment to our business reputation;
- withdrawal of clinical study participants;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- the inability to commercialize our products; and
- loss of revenues.

We carry product liability insurance for our clinical studies. Further, we intend to expand our insurance coverage to include the sale of commercial products if marketing approval is obtained for any of our product candidates. However, we may be unable to obtain this product liability insurance on commercially reasonable terms and with insurance coverage that will be adequate to satisfy any liability that may arise. On occasion, large judgments have been awarded in class action or individual lawsuits relating to marketed pharmaceuticals. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

The success of our business depends primarily upon our ability to identify, develop and commercialize product candidates. Because we have limited financial and managerial resources, we focus on specific product candidates for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or other indications that later prove to have greater commercial potential. We may focus our efforts and resources on product candidates that ultimately prove to be unsuccessful.

If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights.

Risks Related to Our Intellectual Property

If we are unable to obtain or protect intellectual property rights related to our products and product candidates, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our products and product candidates. The strength of patents in the biotechnology

and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own,co-own or in-license may fail to result in issued patents with claims that cover the products in the United States or in other countries. If this were to occur, early generic competition could be expected against our products. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which if it exists could be used to invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue, third parties may challenge their validity, enforceability, scope or ownership, which may result in such patents, or our rights to such patents, being narrowed or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. If the patent applications we hold or license with respect to our product candidates fail to issue or if their breadth or strength of protection is threatened, it could dissuade companies from collaborating with us and threaten our ability to commercialize our products. We cannot offer any assurances about which, if any, patents will issue or whether any issued patents will be found invalid or unenforceable, will be challenged by third parties or will adequately protect our products. Further, if we encounter delays in development or regulatory approvals, the period of time during which we could market our products under patent protection could be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we or our licensors were the first to file any patent application related to our product candidates. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be started by a third party or instituted by us to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license it from the prevailing party, which may not be available on commercially reasonable terms or at all.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietaryknow-how that is not patentable, processes for which patents are difficult to enforce and other elements of our drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. Although we expect all of our employees to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed, that such agreements provide adequate protection and will not be breached, that our trade secrets and other confidential proprietary information will not otherwise be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

Further, the laws of some foreign countries do not protect patents and other proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property abroad. We may also fail to pursue or obtain patents and other intellectual property protection relating to our products and product candidates in all foreign countries.

Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts or otherwise affect our business.

Our commercial success depends in part on our avoiding infringement and other violations of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and inter party re-examination proceedings before the United States Patent and Trademark Office (U.S. PTO) and its foreign counterparts. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. As the biotechnology and pharmaceutical

industries expand and more patents are issued, and as we gain greater visibility and market exposure as a public company, the risk increases that our product candidates or other business activities may be subject to claims of infringement of the patent and other proprietary rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product unless we obtained a license under the applicable patents, or until such patents expire. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy, the holders of any such patent may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all. In addition, we may be subject to claims that we are infringing other intellectual property rights, such as trademarks or copyrights, or misappropriating the trade secrets of others, and to the extent that our employees, consultants or contractors use intellectual property or proprietary information owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. We are currently engaged in legal proceedings with Genfit S.A., which alleges that we misappropriated some of their trade secrets.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful infringement or other intellectual property claim against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our affected products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize one or more of our product candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist that might be enforced against our products or product candidates, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties.

We license certain key intellectual property from third parties, and the loss of our license rights could have a materially adverse effect on our business.

We are a party to a number of technology licenses that are important to our business and may enter into additional licenses in the future. For example, we rely on an exclusive license to certain patents and know-how from Janssen Pharmaceutical NV (Janssen NV), which include seladelpar and certain other PPARd compounds (the PPARd Products). Under the exclusive license with Janssen NV we have full control and responsibility over the research, development and registration of any PPARd Products and are required to use diligent efforts to conduct all such activities. If we fail to comply with our obligations under our agreement with Janssen NV, including our obligations to expend more than a de minimis amount of effort and resources on the research and/or development of at least one PPARd Product, to make any payment called for under the agreement, not to

disclose any non-exempt confidential information related to the agreement, or to use diligent efforts to promote, market and sell any PPARδ Product under the agreement, such action would constitute a default under the agreement and Janssen NV may have the right to terminate the license, in which event we would not be able to develop or market products covered by the license, including in the case of the Janssen NV license, seladelpar, which would have a materially adverse effect on our business.

We may be involved in lawsuits to protect or enforce our patents, the patents of our licensors or our other intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors may infringe or otherwise violate our patents, the patents of our licensors or our other intellectual property rights. To counter infringement or unauthorized use, we may be required to file legal claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is invalid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing. The initiation of a claim against a third party may also cause the third party to bring counter-claims against us.

We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Our business could be harmed if in a litigation the prevailing party does not offer us a license on commercially reasonable terms. Any litigation or other proceedings to enforce our intellectual property rights may fail, and even if successful, may result in substantial costs and distract our management and other employees.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the U.S. PTO and foreign patent agencies in several stages over the lifetime of the patent. The U.S. PTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors that control the prosecution and maintenance of our licensed patents fail to maintain the patents and patent applications covering our product candidates, we may lose our rights and our competitors might be able to enter the market, which would have a material adverse effect on our business.

Risks Related to Our Business Operations and Industry

Our business could be negatively affected as a result of the actions of activist or hostile stockholders.

Our business could be negatively affected as a result of stockholder activism, which could cause us to incur significant expense, hinder execution of our business strategy, and impact the trading value of our securities. For

example, on April 27, 2020, a stockholder filed a preliminary proxy statement containing proposed opposition to our preliminarily filed proxy statement on April 27, 2020, including a proposal to elect three new directors to our Board of Directors and a proposal not to increase to the number of shares of common stock authorized for issuance. While this proxy contest was subsequently suspended, stockholder activism could recur and requires significant time and attention by management and the Board of Directors, potentially interfering with our ability to execute our strategic plan. Stockholder activism could give rise to perceived uncertainties as to our future direction, adversely affect our relationships with key executives and business partners, and make it more difficult to attract and retain qualified personnel. Also, we may be required to incur significant legal fees and other expenses related to activist stockholder matters. Any of these impacts could materially and adversely affect our business and operating results. Further, the market price of our common stock could be subject to significant fluctuation or otherwise be adversely affected by stockholder activism.

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are dependent on principal members of our executive team. While we have entered into employment offer letters with each of our executive officers, any of them could leave our employment at any time, as all of our employees are "at will" employees. We do not maintain "key person" insurance for any of our executives or other employees. Recruiting and retaining other qualified employees for our business, including clinical, scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives in our industry, which is likely to continue. We also experience competition from universities, competitors and research institutions for the hiring of scientific and clinical personnel. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. In addition, failure of any of our clinical studies may make it more challenging to recruit and retain qualified personnel. If we are unable to successfully recruit key employees or replace key executives or key employees, it may adversely affect the progress of our research, development and commercialization objectives.

In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategies. Our consultants and advisors may be engaged by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us, which could also adversely affect the progress of our research, development and commercialization objectives.

As we continue to build our clinical and drug development operations, we will need to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

As we continue to build our clinical development programs, we are expanding our employee base to increase our managerial, clinical, scientific, and other operational teams. Such growth imposes additional responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors. Also, our management may need to divert a greater amount of attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among current employees. Our expected growth could require greater capital expenditures and may divert financial resources from other projects, such as the development of product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to create value and/or generate revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to develop and commercialize seladelpar and other potential product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

Significant disruptions of information technology systems or breaches of data security could materially adversely affect our business, results of operations and financial condition.

We collect and maintain information in digital form that is necessary to conduct our business, and we are increasingly dependent on information technology systems and infrastructure to operate our business, particularly in view of the ongoing COVID-19 pandemic and remote work requirements. In the ordinary course of our business, we collect, store and transmit confidential information, including intellectual property, proprietary business information and personal information. It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. We have established physical, electronic and organizational measures to safeguard and secure our systems to prevent a data compromise, and rely on commercially available systems, software, tools, and monitoring to provide security for our information technology systems and the processing, transmission and storage of digital information. We have also outsourced elements of our information technology infrastructure, and as a result a number of third-party vendors may or could have access to our confidential information. Our internal information technology systems and infrastructure, and those of our current and any future collaborators, contractors and consultants and other third parties on which we rely, are vulnerable to damage from computer viruses, malware, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization.

The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. In addition, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information or other intellectual property. The costs to us to mitigate network security problems and security vulnerabilities could be significant, and our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position. If such an event is to occur and cause interruptions in our operations or our vendors, it may result in a material disruption of our product development programs and our reputation could be materially damaged. We could also be exposed to a risk of loss or litigation and potential liability, which could materially adversely affect our business, results of operations and financial condition.

Changes in and failures to comply with United States and foreign privacy and data protection laws, regulations and standards may adversely affect our business, operations and consolidated financial performance.

We are subject to or affected by numerous federal, state and foreign laws and regulations, as well as regulatory guidance, governing the collection, use, disclosure, retention, and security of personal data, such as information that we collect about patients and healthcare providers in connection with clinical trials in the United States and abroad. The global data protection landscape is rapidly evolving, and implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future. This evolution may create uncertainty in our business, affect our or our vendors' ability to operate in certain jurisdictions or to collect, store, transfer, use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulation, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, diversion of management time and effort and proceedings against us by governmental entities or others. In many jurisdictions, enforcement actions and consequences for noncompliance are rising.

In the United States, HIPAA imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. Certain states have also

adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. In the event that we are subject to HIPAA or other United States privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition. Our operations abroad may also be subject to increased scrutiny or attention from data protection authorities. Many countries in these regions have established or are in the process of establishing privacy and data security legal frameworks with which we, our customers, or our vendors must comply. For example, the EU has adopted the General Data Protection Regulation (EU) 2016/679, or GDPR, which went into effect in May 2018 and introduces strict requirements for processing the personal information of EU subjects, including clinical trial data. The GDPR has increased compliance burdens on us, including by mandating potentially burdensome documentation requirements and granting certain rights to individuals to control how we collect, use, disclose, retain and process information about them. The processing of sensitive personal data, such as physical health condition, has imposed heightened compliance burdens under the GDPR and is a topic of active interest among foreign regulators. In addition, the GDPR provides for robust regulatory enforcement and fines for a noncompliant company. As we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business.

Risks Relating to Owning Our Common Stock

An active trading market for our common stock may not continue and the market price for our common stock may decline in value.

Our common stock has historically been listed on the Nasdaq Capital Market under the symbol “CBAY” and in the second quarter of 2018 it began trading on the Nasdaq Global Select Market. Historically, trading volume for our common stock has been limited. The historical trading prices of our common stock on the Nasdaq Capital Market and the Nasdaq Global Select Market may not be indicative of the price levels at which our common stock will trade in the future, and we cannot predict the extent to which investor interest in us generally will continue to support an active public trading market for our common stock or how liquid will be that public market.

Our stock price is volatile, and our stockholders’ investment in our stock could decline in value.

The historical trading price of our common stock has been volatile. Our stock price may continue to be subject to wide fluctuations in response to a variety of factors, including:

- delays in enrolling and/or completing the RESPONSE clinical trial or our other clinical trials;
- adverse or inconclusive results in our clinical trials;
- adverse or inconclusive results or delays in preclinical testing;
- inability to obtain additional funding;
- any delay in filing an Investigational New Drug (IND) application or NDA for any of our future product candidates and any adverse development or perceived adverse development with respect to the FDA’s review of an IND or NDA;
- failure to enter into new collaborations;
- failure by us or our licensors to prosecute, maintain or enforce our intellectual property rights;
- failure to successfully develop and commercialize our future product candidates;
- changes in laws or regulations applicable to future products;

- changes in the structure of health care payment systems;
- inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products, services or technologies by our competitors;
- failure to meet or exceed financial projections we may provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- announcements of significant or potential equity or debt sales by us;
- announcements of clinical trial plans or results by us or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;
- changes in the market valuations of similar companies;
- sales of our common stock by us or our stockholders in the future; and
- trading volume of our common stock.

In addition, companies trading in the stock market in general have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

Significant additional capital may be needed in the future to continue our product development efforts in current and future clinical trials and operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If in the future we sell common stock, convertible securities or other equity securities, investors may be materially diluted by subsequent sales. These sales may also result in new investors gaining rights superior to our existing stockholders. Pursuant to our equity incentive plans, we are authorized to grant stock options and other equity-based awards to our employees, directors and consultants. The number of shares available for future grant under our equity incentive plans as of December 31, 2021 was 1,588,613 shares.

Anti-takeover provisions in our 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 certificate of incorporation and our bylaws may delay or prevent an acquisition of us. In addition, 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, who are responsible for appointing the members of our management team. In addition, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits, with some exceptions, stockholders owning in excess of 15% of our outstanding voting stock from merging or combining with us. Finally, our charter documents establish advance notice requirements for nominations for election to our board of directors and for proposing matters that can be acted upon at stockholder meetings. Although we believe these provisions together provide for an opportunity to receive higher bids by requiring potential acquirers to negotiate with our board of directors, they would apply even if the offer may be considered beneficial by some stockholders.

General Risks

We do not anticipate paying cash dividends, and accordingly, stockholders must rely on stock appreciation for any return on their investment.

We do not anticipate paying cash dividends in the future. As a result, only appreciation of the price of our common stock, which may never occur, will provide a return to stockholders. Investors seeking cash dividends should not invest in our common stock.

We may be subject to securities litigation, which is expensive and could divert management attention.

Our share price is volatile, and in the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

Our corporate office is located in Newark, California. Our office lease for that facility terminates on January 15, 2024 and has an option to extend the lease for an additional five years. We believe that our current facilities are sufficient for our needs for the foreseeable future.

Item 3. Legal Proceedings

Genfit Litigation

On January 15, 2021, Genfit S.A. (Genfit) filed a complaint against us in the U.S. District Court for the Northern District of California, alleging misappropriation of trade secrets and related causes of action based on our receipt of a Genfit protocol synopsis for Genfit's Phase 3 clinical trial of its drug candidate elafibranor in patients with primary biliary cholangitis. An Amended Complaint was filed on April 16, 2021 with substantially the same allegations. Genfit seeks damages in an unspecified amount as well as injunctive relief. We have stated in pleadings that we did not request or take any steps to obtain Genfit's protocol synopsis, have taken diligent steps to remove and quarantine it, and are not using any Genfit trade secrets in our clinical trials. On March 12, 2021, the court granted a Temporary Restraining Order (later converted to a Preliminary Injunction), prohibiting us from accessing or disseminating the protocol synopsis, using any Genfit trade secrets contained therein or destroying any evidence related thereto. We filed a Motion to Dismiss the Amended Complaint that was granted on September 9, 2021, with leave to amend. Genfit filed a Second Amended Complaint on October 15, 2021 with

substantially the same allegations and claims for relief as in the original complaint. We filed a Motion to Dismiss the Second Amended Complaint that was granted on January 21, 2022, without further leave to amend. What remains in the complaint is an alleged misappropriation of the protocol synopsis as a whole. We filed our Answer to what remained of the Second Amended Complaint on February 4, 2022. We intend to defend ourselves vigorously.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market for Common Equity

Our common stock is listed on the Nasdaq Global Select Market under the symbol "CBAY". As of February 28, 2022, there were approximately 221 holders of record of our common stock, although there are a substantially greater number of "beneficial holders," whose shares are held of record by banks, brokers and other financial institutions in "street name."

Dividend Policy

We have never declared or paid any cash dividends to our stockholders. Our board of directors will make any future decisions regarding dividends. We currently intend to retain and use any future earnings, if any, for the development and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Under our Development Financing Agreement with Abingworth we are not permitted to pay dividends without the consent of Abingworth. Except for the restrictions under our agreement with Abingworth, our board of directors has complete discretion on whether to pay dividends. Even if our board of directors is able to and decides to pay dividends, the form, frequency and amount will depend upon our future operations and earnings, capital requirements and surplus, general financial condition, contractual restrictions and other factors that the board of directors may deem relevant.

Item 6. [Reserved]

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

Forward-Looking Statements

Some of the statements under in this "Management's Discussion and Analysis of Financial Condition and Results of Operations" are forward-looking statements. See "Cautionary Language Regarding Forward Looking Statements" at the beginning of this Annual Report for cautionary information regarding forward-looking statements. These statements appear throughout this Annual Report on Form 10-K and are statements regarding our current expectation, belief, or intent, primarily with respect to our operations and related industry developments. Examples of these statements include, but are not limited to, statements regarding our expectations with respect to the following: our business and scientific strategies; the progress of our product development programs, and the timing of results thereof; regulatory submissions and approvals; the impact of the COVID-19 pandemic, including the emergence of COVID-19 variants such as the Delta and Omicron variants, on our company and operations; the anticipated benefits of our development financing agreement with Abingworth; our drug discovery technologies; our research and development expenses; protection of our intellectual property; sufficiency of our cash and capital resources and the need for additional capital; and our operations and legal risks. You should not place undue reliance on these forward-looking statements. Our actual

results and the timing of events may differ significantly from the results discussed in the forward-looking statements for many reasons. Factors that might cause such a difference include those discussed under the caption "Risk Factors" and elsewhere in this Annual Report on Form 10-K. These and many other factors could affect our future financial and operating results. We undertake no obligation to update any forward-looking statement to reflect events after the date of this Annual Report.

Overview

CymaBay Therapeutics, Inc. is a clinical-stage biopharmaceutical company focused on developing and providing access to innovative therapies for patients with liver and other chronic diseases with high unmet medical need.

Our lead product candidate, seladelpar, is a potent and selective agonist of peroxisome proliferator activated receptor delta (PPARd), a nuclear receptor that regulates genes directly or indirectly involved in the synthesis of bile acids/sterols, metabolism of lipids and glucose, inflammation, and fibrosis. We have been focused on developing seladelpar for the treatment of primary biliary cholangitis (PBC), an autoimmune disease that causes progressive destruction of the bile ducts in the liver resulting in impaired bile flow (cholestasis) and inflammation.

In late 2019, we terminated our ongoing PBC studies and other seladelpar-related studies that were ongoing at that time. Specifically, the decision to halt development of seladelpar was based on initial histological observations seen in our Phase 2b study of seladelpar in patients with NASH that were observed in the first blinded tranche of end-of-treatment liver biopsies in that trial. Thereafter, in December 2019, we announced a restructuring plan to reduce our workforce by approximately 60% to control our operating costs, pending further investigation of the histological observations. In May 2020, an independent expert panel completed a review of the findings and unanimously concluded that the data in aggregate did not support liver injury related to seladelpar. We subsequently discussed the data, the panel's conclusions, and other matters with the FDA and in July 2020, the FDA lifted the clinical hold, thereby permitting us to reinstate clinical development of seladelpar. Specifically, we made the strategic decision to refocus our strategy primarily on clinical development of seladelpar in PBC.

Seladelpar—Primary Biliary Cholangitis (PBC)

Following the decision to reinstate clinical development of seladelpar, in late 2020, we commenced startup and site feasibility activities for RESPONSE, a new global Phase 3 registration study to evaluate seladelpar in patients with PBC. The RESPONSE trial is actively recruiting and enrolling patients.

In addition to RESPONSE we also commenced startup activities in late 2020 for ASSURE, a new long-term safety study, which is open to patients who were eligible for our previous long-term extension study that was terminated early in late 2019, including those patients from our previously completed Phase 2 open label study and our Phase 3 ENHANCE study, as well as patients who complete treatment in RESPONSE in the future. The ASSURE trial is actively enrolling patients.

MBX-2982

MBX-2982 targets G protein-coupled receptor 119 (GPR119), a receptor that interacts with bioactive lipids known to stimulate glucose-dependent insulin secretion. In November 2020, we announced a study to evaluate the potential for MBX-2982 to stimulate the release of the hormone glucagon in response to hypoglycemia in patients with type 1 diabetes (T1D). The Phase 2a proof-of-pharmacology study will assess whether MBX-2982 can enhance glucagon secretion during insulin-induced hypoglycemia in subjects with T1D. The study is actively enrolling patients. If successful, studies to evaluate MBX-2982 as a potential preventive therapy for hypoglycemia in patients with T1D may be warranted. The study is being led by the AdventHealth Translational

Research Institute in Orlando, Florida and is fully funded by The Leona M. and Harry B. Helmsley Charitable Trust. CymaBay retains full commercial rights to MBX-2982. We believe MBX-2982 may also have utility in various inflammatory diseases and we are currently exploring potential opportunities to advance development.

CB-0406

In 2020 we began to evaluate CB-0406, the active metabolite of arhalofenate, a pro-drug previously studied for chronic metabolic diseases, in a single and multiple ascending dose study in healthy subjects to establish its pharmacokinetics, safety and maximum tolerated dose. While the study showed CB-0406 had improved pharmacokinetics versus arhalofenate, CB-0406's safety profile did not support continued development as a result of the occurrence of a small number of reversible cases of thrombocytopenia at higher doses. Therefore, in mid-2021 we discontinued development of CB-0406.

COVID-19 Pandemic

As a result of the COVID-19 pandemic, we have experienced and may continue to experience disruptions that could impact aspects of our business, including our progress towards the initiation and completion of certain clinical studies, and other associated drug development activities. The emergence of COVID-19 variants, such as the Delta, and Omicron variants, have further disrupted, and may continue to disrupt, aspects of our business, in particular in regard to the initiation and operation of clinical trial sites in portions of the United States, in the U.K and in Europe. Possible future disruptions are currently difficult to foresee. We continue to monitor areas of potential risk which include, but are not limited to, the following:

- Clinical trial and drug manufacturing operations—In collaboration with our clinical research organization partners, we sponsor clinical trials that take place at investigator sites in the U.S. and internationally. We also partner with contract manufacturing organizations to develop, manufacture, and distribute our product candidate drug supplies. To date, these collective research and development personnel and vendors have adapted to COVID-19 related travel restrictions and reduced access to work facilities through the use of remote working technologies and other measures as they continue to progress toward completion of our clinical trials. However, as we continue to enroll clinical trials and look to complete the clinical development of seladelpar and initiate other programs, our research and development employees and contractors may not be able to sufficiently access their applicable work facilities as a result of continued facility closure orders and the possibility that governmental authorities might further modify such restrictions. Furthermore, Although we and our contractors continue to plan for and develop pandemic-related risk mitigation strategies, it is uncertain whether these plans will continue to be sufficient to fully offset the potential impact COVID-19, including the emergence of new COVID-19 variants, travel restrictions and/or facility access restrictions (or other unanticipated impediments) may have on our ability to execute our development activities in a timely and cost-effective manner.
- Drug regulator interactions—The FDA and comparable foreign regulatory agencies may experience operational interruptions or delays, which could impact timelines for regulatory meetings, submissions, trial initiations, and regulatory approvals. For example, COVID-19 related regulatory submission issues have created an impediment to clinical site activation in the U.K.
- Financial reporting and compliance—To date, there has been no adverse impact on our ability to maintain our established financial reporting functions and internal controls over financial reporting. However, our ability to prepare our financial results timely and accurately is partially dependent upon the availability of third-party information systems and other cloud-based services.
- Remote workforce operations—To date, our workforce has adapted to remotely working to maintain operations. However, remote operations could increase our cyber-security risk, create data accessibility concerns, and make us more susceptible to communication disruptions, any of which could adversely

impact our business operations, or delay necessary interactions with regulators, contract manufacturers, contract research organizations, clinical trial sites, and other important agencies and contractors, which may result in increased costs to us.

Overall, we cannot at this time predict the specific extent, duration, or full impact that the continuing COVID-19 pandemic will have on our future consolidated financial condition and operations. The impact of the COVID-19 pandemic on our consolidated financial performance will depend on future developments, including emergence of COVID-19 variants, such as the Delta and Omicron variants, the duration and spread of the pandemic and related governmental advisories and restrictions, which could result in unexpected costs to us. These developments and the impact of COVID-19 on the financial markets and the overall economy are highly uncertain. If the financial markets and/or the overall economy are impacted for an extended period, our results may be adversely affected.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States (GAAP). The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets and liabilities and disclosure of contingent liabilities at the date of the consolidated financial statements, as well as the reported revenues and expenses during the reporting periods. We base our estimates on historical experience and on various other factors that we believe to be materially reasonable under the circumstances, the results of which form our basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources and evaluate our estimates on an ongoing basis. Actual results may materially differ from those estimates under different assumptions or conditions.

While we describe our significant accounting policies in more detail in *Note 2—Summary of Significant Accounting Policies* of our consolidated financial statements included in this Annual Report, we believe the following accounting policies to be critical to the judgments and estimates used in the preparation and understanding of our consolidated financial statements.

Research and Development Expenses and Related Prepayments and Accruals

Research and development expenses consist of costs incurred in identifying, developing, and testing product candidates. These expenses consist primarily of costs for research and development personnel, including related stock-based compensation; contract research organizations (CRO) and other third parties that assist in managing, monitoring, and analyzing clinical trials; investigator and site fees; laboratory services; consultants; contract manufacturing services; non-clinical studies, including materials; and allocated expenses, such as depreciation of assets, and facilities and information technology that support research and development activities. Research and development costs are expensed as incurred unless there is an alternative future use in other research and development projects.

As part of the process of preparing our consolidated financial statements, we are required to estimate certain research and development expenses. This process involves reviewing contracts, reviewing the terms of our license agreements, communicating with our vendors and applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service either when we have prepaid or when we have not yet been invoiced or otherwise notified of actual cost. Although certain of our vendors require us to prepay in advance of services rendered, the majority of our service providers invoice us monthly in arrears for services performed. We make estimates of prepayments to amortize or expenses to be accrued as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. Such payments are evaluated for current or noncurrent classification based on when they will be realized. Additionally, if expectations change such that we do not expect goods to be

delivered or services to be rendered, such prepayments are charged to expense. Examples of estimated amortized or accrued research and development expenses include fees to:

- contract research organizations and other service providers in connection with clinical studies;
- contract manufacturers in connection with the production of clinical trial materials; and
- vendors in connection with preclinical development activities.

We base our expenses related to clinical studies on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and contract research organizations that conduct and manage clinical studies on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows and expense recognition. Payments under some of these contracts depend on factors such as the successful screening and enrollment of patients and the completion of clinical trial milestones. In either amortizing or accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the related prepayment or accrual accordingly. Our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in our reporting changes in estimates in any particular period. Adjustments to prior period estimates have not been material for the years ended December 31, 2021 and 2020.

Pre-funded Warrants

Pursuant to our public equity offering completed in November 2021, we issued pre-funded warrants to purchase 3,125,000 shares of common stock at a price of $3.9999 per share. These pre-funded warrants have an exercise price of $0.0001 per share, were fully exercisable upon issuance, and have no expiration date. We determined that the pre-funded warrants should be equity classified because they are freestanding financial instruments, are immediately exercisable, do not embody an obligation for us to repurchase its shares, permit the holders to receive a fixed number of shares of common stock upon exercise, are indexed to our common stock and meet the equity classification criteria. In addition, such pre-funded warrants do not provide any guarantee of value or return. Accordingly, the proceeds from the issuance of the warrants were recorded as additional paid-in capital on our consolidated balance sheet as of December 31, 2021.

Development Financing Agreement

We account for the Financing Agreement (see Note 6) as a debt instrument. Accordingly, we have recorded payments received under the Financing Agreement as part of a development financing liability in our consolidated balance sheet. The liability is recorded at amortized cost and accreted to the contractual success fee amounts based on the estimated timing of regulatory approval and attainment of certain sales milestones using an imputed interest rate. Certain transaction fees incurred specifically to complete the Financing Agreement were capitalized and recorded as a reduction to the carrying amount of the development financing liability and are being amortized to interest expense using the effective interest rate method.

There are several factors that could affect the estimated timing of regulatory approval and attainment of sales milestones, some of which are not entirely within our control. Therefore, we periodically reassess the estimated timing of regulatory approval and attainment of sales milestones, and the expected contractual success fee payments due therefrom. If the timing and/or amount of such expected payments is materially different than original estimates, we will prospectively adjust the accretion of the development financing liability and the imputed interest rate.

We identified certain contingent repayment features in the Financing Agreement that are required to be bifurcated from the debt host instrument as embedded derivative liabilities; however, we determined the fair

value of these features, both individually and in aggregate, were immaterial at inception and as of December 31, 2021. The fair value of these features will be assessed at each subsequent reporting date and will be marked to market, if material. To determine the amount to record for the embedded derivative liability, we must assess the probability of occurrence of various potential future events that could affect the timing and/or amount of future cash flows related to the Financing Agreement.

Stock-Based Compensation

We measure stock-based compensation cost at the grant date, based on the estimated fair-value of the awards, and we recognize the portion that we ultimately expect to vest as an expense over the related vesting periods, net of forfeitures. We estimate the grant-date fair value based of stock options using the Black-Scholes option pricing model and recognize compensation expense over the service period using the straight-line attribution method and forfeitures are account for as they occur.

The Black-Scholes option-pricing model requires the input of certain assumptions. These variables include, but are not limited to, our stock price volatility over the term of the awards, and actual and projected employee stock option exercise behaviors. We determine our stock price volatility based on the sufficiency of our historical stock price data. Due to insufficient historical data of exercise behavior, we have used the "simplified method" to determine the expected life of stock options granted with a service condition. Management continually assesses the assumptions and methodologies used to calculate the estimated fair value of stock-based compensation and evaluates the need to make changes when and if necessary. Any such changes to our valuation assumptions and methodologies could materially impact our fair value determination and the resulting stock-based compensation expense.

Results of Operations

General

To date, we have not generated any income from operations. As of December 31, 2021, we have an accumulated deficit of $766.9 million, primarily as a result of expenditures for research and development and general and administrative expenses from inception to that date. All of our product candidates are at various
stages of development and will require additional work and regulatory approval before they can be licensed or commercialized. Accordingly, we expect to continue to incur substantial losses from operations for the foreseeable future and there can be no assurance that we will ever generate sufficient revenue to achieve and sustain profitability. Until we can generate sufficient product revenue, which we may never do, we will need to finance future cash needs through potential collaborative, partnering or other strategic arrangements, as well as through equity offerings, debt financings or a combination of the foregoing.

Operating Results

Our results of operations for the years ended December 31, 2021 and 2020 are presented below (in thousands):

	Year Ended December 31,		Change
	2021	2020	2021 vs 2020
($ in thousands)			
Operating expenses:			
Research and development	$64,542	$35,882	$ 28,660
General and administrative	23,040	16,720	6,320
Total operating expenses	$87,582	$52,602	$ 34,980

	Year Ended December 31,		Change
	2021	2020	2021 vs 2020
Loss from operations	$(87,582)	$(52,602)	$ (34,980)
Other income (expense), net:			
Interest income	167	1,616	(1,449)
Interest expense	(2,583)	—	(2,583)
Total other income (expense), net	(2,416)	1,616	(4,032)
Net loss	$(89,998)	$(50,986)	$ (39,012)

Research & Development Expenses

Conducting research and development is central to our business model. Research and development expenses increased $28.7 million to $64.5 million from $35.9 million for the years ended December 31, 2021 and 2020, respectively. This increase was largely due to activities associated with the development of seladelpar focusing primarily on our late-stage PBC program. In 2020, expenses included costs associated with shutdown of certain clinical trials after the seladelpar program was placed on clinical hold in late 2019 pending further investigation. This investigation was concluded in the second quarter of 2020, the clinical hold was subsequently lifted in July 2020, and we made the decision to restart the seladelpar development program in July 2020. As we continue to progress late-stage development of seladelpar in PBC as well as development activities associated with other product candidates, we expect research and development costs to continue to increase in the future.

Research and development expenses are detailed further in the table below (in thousands):

	Year Ended December 31,		Change
	2021	2020	2021 vs 2020
Project costs:			
Seladelpar PBC clinical studies	$35,007	$15,747	$ 19,260
Seladelpar drug manufacturing & development	5,531	1,332	4,199
Seladelpar other studies	549	2,440	(1,891)
Non-seladelpar studies	2,647	3,374	(727)
Total project costs	43,734	22,893	20,841
Internal research and development costs	20,808	12,989	7,819
Total research and development	$64,542	$35,882	$ 28,660

Our project costs consist primarily of:

- expenses incurred under agreements with contract research organizations and investigative sites that conduct our clinical trials and a substantial portion of our preclinical activities;
- the cost of acquiring materials and manufacturing drug products for use in clinical trial and other research activities; and
- other costs associated with development activities, including additional studies.

Internal research and development costs consist primarily of salaries and related fringe benefits costs for our employees (such as workers' compensation and health insurance premiums), stock-based compensation charges, travel costs, consulting, other outside services and overhead expenses. Internal costs generally benefit multiple projects and are not separately tracked per project.

Total project costs increased by $20.8 million to $43.7 million from $22.9 million for the years ended December 31, 2021 and 2020, respectively. Project costs for the year ended December 31, 2021 primarily consisted of seladelpar-related clinical trial expenses for PBC. These cost increases were driven primarily by an

expansion of our site activation, patient enrollment, and other clinical trial activities following our decision to restart development of the seladelpar program in July 2020 after the FDA lifted the clinical hold on seladelpar. Internal research and development costs increased by $7.8 million to $20.8 million from $13.0 million for the years ended December 31, 2021 and 2020, respectively, primarily due to higher employee compensation incurred in the year ended December 31, 2021 as compared to the year ended December 31, 2020, as we hired additional research and development personnel to support the restart of our drug development activities.

General and Administrative Expenses

General and administrative expenses consist principally of personnel-related costs, professional fees for legal, consulting, and accounting services, overhead expenses, and other general operating expenses not otherwise included in research and development. General and administrative expenses increased by $6.3 million to $23.0 million, from $16.7 million, for the years ended December 31, 2021 and 2020, respectively. The increase was driven primarily by the hiring of additional general and administrative personnel, consultant and other expenses in the second half of 2020 after we made the decision to restart our development activities. We expect general and administrative expenses to continue to increase in the future as we continue to add administrative personnel and expand our infrastructure in support of our drug development activities.

Other Income (Expense), Net

Other income consists of interest income from our marketable securities. Interest income decreased to $0.2 million from $1.6 million for the years ended December 31, 2021 and 2020, respectively. The decrease of $1.4 million was due to lower prevailing interest rates and a reduced investment portfolio balance, on average, compared to prior year.

Interest expense is related to the accretion of the development financing liability recorded in connection with the July 2021 Abingworth Development Financing Agreement using the effective interest method, and totaled $2.6 million for the year ended December 31, 2021. No interest expense was incurred for the year ended December 31, 2020.

Income Taxes

As of December 31, 2021, we had federal net operating loss carryforwards of $522.7 million and state net operating loss carryforwards of $288.3 million to offset future taxable income, if any. In addition, we had federal research and development tax credit carryforwards of $10.2 million, federal orphan drug tax credit carryforwards of $24.8 million, and state research and development tax credit carryforwards of $6.2 million. If not utilized, the federal net operating losses for the years beginning before January 1, 2018 of $255.7 million will expire beginning in 2024 through 2037, and the federal net operating losses for the tax years beginning after January 1, 2018 of $267.0 million will be carried forward indefinitely (subject to certain utilization limitations). The state net operating loss carryforwards will expire beginning in 2028 through 2041. The federal research and development and federal orphan drug tax credit carryforwards expire 2021 through 2041, and the state tax credit will carry forward indefinitely. Interest and penalties for the years ended December 31, 2021 and 2020 were not material. Current federal and state tax laws include substantial restrictions on the utilization of net operating losses and tax credits in the event of an ownership change. Even if the carryforwards are available, they may be subject to annual limitations, lack of future taxable income, or future ownership changes that could result in the expiration of the carryforwards before they are utilized. At December 31, 2021, we recorded a 100% valuation allowance against our deferred tax assets of approximately $173.9 million, as our management believes it is more likely than not that they will not be fully realized.

Liquidity and Capital Resources

We have financed our operations primarily through the sale of equity securities, licensing fees, issuance of debt and collaborations with third parties. As of December 31, 2021, cash, cash equivalents and marketable securities totaled $194.6 million, compared to $146.3 million at December 31, 2020.

Development Financing

On July 30, 2021, (the Effective Date) we entered into a Development Financing Agreement (the Financing Agreement) with Abingworth to obtain funding to support our development of seladelpar for the treatment of PBC. The Financing Agreement provides us up to $100.0 million in funding, of which $25 million was received in August 2021, $25 million was received in November 2021 and $25 million was subsequently received in January 2022. We also have an option to draw an additional $25 million (the Optional Funding) within approximately two months of the completion of enrollment of our Phase 3 RESPONSE clinical trial. The Optional Funding is subject to certain customary funding conditions. In return, we will pay to Abingworth fixed and variable success payments, as further described in *Note 6—Development Financing Agreement* in the notes to our consolidated financial statements in Part IV, Item 15 of this Annual Report on Form 10-K. The Development Financing Agreement also provides that we must raise additional funds in a public or private offering within nine months of the Effective Date of the agreement. This capital raise requirement was met following the completion of our public equity offering discussed below.

We were in compliance with all terms and covenants related to the Financing Agreement as of December 31, 2021.

Sale of Common Stock and Pre-funded Warrants

On November 22, 2021, we sold 15,625,000 shares of common stock at $4.00 per share and pre-funded warrants to purchase 3,125,000 shares of common stock at $3.9999 per share in a public equity offering, for total gross offering proceeds of approximately $75 million, before deducting the underwriting commissions and other estimated offering expenses. We also granted the underwriters of the offering a 30-day option to purchase up to an additional 2,812,500 shares of its common stock at the public offering price per share less underwriting commissions, which expired unexercised on December 22, 2021. The proceeds of the offering, net of offering expenses, were $70.5 million. We anticipate using the net proceeds from the offering to fund ongoing development of seladelpar and for working capital and general corporate purposes.

At-the-Market (ATM) Facility

In July 2020, we filed a $200.0 million registration statement on Form S-3 with the SEC and entered into an at-the-market facility (ATM) to sell up to $75.0 million of common stock under the registration statement. To date, we have not sold any shares of common stock under the ATM.

Cash Flows

The following table sets forth a summary of the net cash flow activity for each of the periods indicated below (in thousands):

	Year Ended December 31,	
	2021	**2020**
Net cash used in operating activities	$ (69,431)	$(44,725)
Net cash provided by investing activities	48,589	47,957
Net cash provided by financing activities	118,455	92
Net increase in cash and cash equivalents	$ 97,613	$ 3,324

Cash Flows from Operating Activities

Cash used in operating activities for the year ended December 31, 2021 increased by $24.7 million to $69.4 million as compared to $44.7 million in the prior year. The increase in cash used was primarily due to a

$39.0 million increase in our net loss to $90.0 million from $51.0 million in the prior year period as a result of our reinstatement of our seladelpar development program. This effect was also impacted to a lesser extent by changes in our working capital.

Cash Flows from Investing Activities

Cash provided by investing activities was $48.6 million for the year ended December 31, 2021 compared to $48.0 million of cash used in the prior year, primarily due to the timing of our investments in marketable securities.

Cash Flows from Financing Activities

Cash provided by financing activities was $118.5 million for the year ended December 31, 2021 compared to $0.1 million in the prior year. The increase was primarily due to net proceeds of $70.5 million received from the November 2021 public equity offering and net proceeds of $47.7 million from the Financing Agreement with Abingworth.

Capital Requirements

We have incurred operating losses since inception and had an accumulated deficit of $766.9 million at December 31, 2021. As of December 31, 2021, we had cash, cash equivalents and marketable securities of approximately $194.6 million, which we believe is sufficient, together with committed capital, to fund our current operating plan through 2023.

We expect to continue to incur substantial expenses related to our development activities for the foreseeable future as we continue product development for seladelpar. Since product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later stage clinical trials, we expect that our research and development expenses will increase in the future. We will therefore continue to require additional financing to develop our products and fund future operating losses and will seek funds through equity financings, debt, collaborative or other arrangements with corporate sources, or through other sources of financing. It is unclear if or when any such financing transactions will occur, on satisfactory terms or at all. Our failure to raise capital as and when needed could have a negative impact on our financial condition and our ability to pursue our business strategies. If adequate funds are not available to us, it could have a material adverse effect on our business, results of operations, and financial condition.

Contractual Obligations and Other Cash Requirements

Our long-term contractual obligations as of December 31, 2021 include primarily $1.3 million for our corporate office facility lease, which includes monthly rental payments that are payable through January 2024, the lease termination date. We are also obligated to reimburse the lessor for a prorated portion of monthly facility operating expenses during the lease term.

In addition, we rely on contract research organizations and other research support providers to perform clinical and preclinical studies for us and we contract with firms to supply our drug compounds for use in our development activities. Under the terms of our agreements with these organizations, we are obligated to make future payments as services are provided. However, these agreements are terminable by us upon written notice and we are generally only liable for actual effort expended or cost incurred by the organizations through the termination notice period.

We also have significant potential payment obligations under the Financing Agreement that are contingently payable by us to Abingworth upon regulatory approval of seladelpar in PBC and achievement of certain sales for seladelpar.

We also have certain potential in-license obligations that are contingently payable by us to licensors upon our achievement of certain development and commercialization milestones for our product candidates.

Finally, in the normal course of business, we enter into various firm purchase commitments and other contractual obligations, which are cancelable within ninety days or less.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Not applicable.

Item 8. Financial Statements and Supplementary Data

The disclosure required in this Item is included in Item 15, which information is incorporated by reference here.

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

None.

Item 9A. *Controls and Procedures*

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our reports under the Exchange Act, and the rules and regulations thereunder, 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 our management, including our chief executive officer and principal financial officer, as appropriate, to allow for timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Based on the evaluation of our disclosure controls and procedures (as defined in Rules13a-15(e) and 15d-15(e) under the Exchange Act), our chief executive officer and principal financial officer have concluded that, as of the end of the period covered by this report, the design and operation of our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is a process designed by, or under the supervision of, our President and Chief Executive Officer and our Vice President, Finance to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that (1) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Under the supervision and with the participation of our management, including our President and Chief Executive Officer and Vice President, Finance, we conducted an evaluation of the effectiveness of our internal

control over financial reporting based on criteria established in "Internal Control—Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on this evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2021.

As a non-accelerated filer, we are not required to obtain an opinion of our independent auditors with respect to our internal controls over financial reporting for the period ended December 31, 2021.

Limitations on the Effectiveness of Controls

A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the controls are met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues, if any, within a company have been detected. Accordingly, our disclosure controls and procedures are designed to provide reasonable, not absolute, assurance that the objectives of our disclosure control system are met.

Changes in Internal Controls

There were no changes in our internal control over financial reporting that occurred during the quarter ended December 31, 2021, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. ***Other Information***

As earlier stated, on July 30, 2021, we entered into a Development Financing Agreement (the Financing Agreement) with ABW Cyclops SPV LP, an affiliate of Abingworth LLP (Abingworth), pursuant to which Abingworth provided us with $75 million of funding to support our development of seladelpar for the treatment of PBC. In 2021 we received $50.0 million of this amount, and received an additional $25.0 million in January 2022.

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

Not applicable.

PART III

Item 10. ***Directors, Executive Officers and Corporate Governance***

The information required by this item with respect to our executive officers is incorporated herein by reference to the information set forth under the caption "Information about our Executive Officers" in Part I of this Annual Report. The information required by this item with respect to our directors is incorporated herein by reference to the information set forth under the caption "Proposal I–Election of Directors" in our proxy statement for our 2022 annual meeting of stockholders, or the 2022 Proxy Statement. The information required by this item with respect to late Section 16 filings is incorporated by reference to the information set forth under the caption "Delinquent Section 16(a) Reports" in the 2022 Proxy Statement. The information required by this item with respect to the committees of our board of directors is incorporated by reference to the information set forth under the caption "Information Regarding the Board of Directors and Corporate Governance–Information Regarding Committees of the Board" in the 2022 Proxy Statement.

If the 2022 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report onForm 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

Code of Business Conduct

Our Code of Business Conduct and Ethics applies to all officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A copy of our Code of Business Conduct and Ethics can be found on our website, http://ir.cymabay.com/governance-docs. The contents of our website are not a part of this Annual Report on Form 10-K. We intend to satisfy the disclosure requirement under Item 5.05 of Form 8-K regarding an amendment to, or waiver from, a provision of this Code of Business Conduct and Ethics by posting such information on our website, at the address and location specified above.

Item 11. ***Executive Compensation***

Reference is made to the information to be included under the heading "Executive Compensation" in our 2022 Proxy Statement, which information is hereby incorporated by reference.

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

The information required by this item will be set forth in our 2022 Proxy Statement under the caption "Security Ownership of Certain Beneficial Owners and Management" and is incorporated herein by reference.

Equity Compensation Plan Information

Information concerning our equity compensation plans will be set forth in our 2022 Proxy Statement under the caption "Securities Authorized for Issuance under Equity Compensation Plans—Equity Compensation Plan Information" and is incorporated herein by reference.

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

The information required by this item will be set forth in our 2022 Proxy Statement under the captions "Transactions with Related Persons" and "Information Regarding the Board of Directors and Corporate Governance—Independence of the Board of Directors" and is incorporated herein by reference.

Item 14. ***Principal Accountant Fees and Services***

The information required by this item will be set forth in our 2022 Proxy Statement under the caption "Principal Accountant Fees and Services" in the proposal under the caption "Ratification of Selection of Independent Registered Public Accounting Firm" and is incorporated herein by reference.

PART IV

Item 15. ***Exhibits and Financial Statement Schedules***

(a) Documents filed as part of this report

1. Financial Statements

2. Financial Statement Schedules

Financial statement schedules have been omitted in this report because they are not applicable, not required under the instructions, or the information requested is set forth in the consolidated financial statements or related notes thereto.

(b) List of Exhibits

The following exhibits are included herein or incorporated herein by reference:

Exhibit No.	Description of Document
3.1	Amended and Restated Certificate of Incorporation. (Filed with the SEC as Exhibit 3.1 to our Amendment No. 2 to Registration Statement on Form 10, filed with the SEC on October 17, 2013, SEC File No. 000-55021.)
3.2	Certificate of Amendment to Amended and Restated Certificate of Incorporation (Filed with the SEC as Exhibit 3.1 to our Current Report on Form 8-K, filed with the SEC on June 26, 2020, SEC File No.001-36500).
3.3	Amended and Restated By-Laws. (Filed with the SEC as Exhibit 3.2 to our Amendment No. 2 to Registration Statement on Form 10, filed with the SEC on October 17, 2013, SEC File No. 000-55021.)
4.1	Reference is made to Exhibits 3.1, 3.2 and 3.3.
4.2	Description of Common Stock. (Filed with the SEC as Exhibit 4.2 to our Form10-K, filed with the SEC on March 25, 2021, SEC File No. 001-35600.)
10.1*	2003 Equity Incentive Plan. (Filed with the SEC as Exhibit 10.1 to our Registration Statement on Form 10, filed with the SEC on August 12, 2013, SEC File No. 000-55021.)
10.2*	Form of 2003 Equity Incentive Plan Stock Option Agreement. (Filed with the SEC as Exhibit 10.2 to our Registration Statement on Form 10, filed with the SEC on August 12, 2013, SEC File No. 000-55021.)
10.3*	Form of 2003 Equity Incentive Plan Early Exercise Stock Option Agreement. (Filed with the SEC as Exhibit 10.3 to our Registration Statement on Form 10, filed with the SEC on August 12, 2013, SEC File No. 000-55021.)
10.4*	2013 Equity Incentive Plan. (Filed with the SEC as Exhibit 10.1 to our Current Report on Form8-K, filed with the SEC on June 7, 2018, SEC File No. 001-36500.)
10.5*	Form of Option Grant Notice and Option Agreement under the 2013 Equity Incentive Plan. (Filed with the SEC as Exhibit 10.26 to our Amendment No. 2 to Registration Statement on Form 10, filed with the SEC on October 17, 2013, SEC File No. 000-55021.)
10.6*	Form of Incentive Award Grant Notice under the 2013 Equity Incentive Plan. (Filed with the SEC as Exhibit 10.22 to our Form10-K, filed with the SEC on March 31, 2014, SEC File No. 000-55021.)
10.7*	2020 New Hire Plan. (Filed with the SEC as Exhibit 10.7 to our Form10-K, filed with the SEC on March 25, 2021, SEC File No. 001-35600.)
10.8*	Form of Stock Option Grant Notice and Option Agreement under the 2020 New Hire Plan. (Filed with the SEC as Exhibit 10.8 to our Form 10-K, filed with the SEC on March 25, 2021, SEC File No.001-35600.)

Exhibit No.	Description of Document
10.9	Form of CymaBay Indemnity Agreement. (Filed with the SEC as Exhibit 10.7 to our Form10-K, filed with the SEC on March 17, 2018, SEC File No 001-36500.)
10.10#	PPAR-d License Agreement, dated June 20, 2006, by and between Metabolex, Inc. and Janssen Pharmaceutical NV. (Filed with the SEC as Exhibit 10.1 to our Form 8-K, filed with the SEC on January 12, 2018, SEC File No.001-36500.)
10.11##	Development Financing Agreement, dated July 30, 2021, by and between CymaBay Therapeutics, Inc. and ABW Cyclops SPV LP. (Filed with the SEC as Exhibit 10.1 to our Form 10-Q, filed with the SEC on November 10, 2021, SEC FileNo. 001-36500.)
10.12	Lease, dated November 8, 2013, between CymaBay Therapeutics, Inc. andBMR-Pacific Research Center, L.P. (Filed with the SEC as Exhibit 10.27 to our Form 10-Q, filed with the SEC on November 25, 2013, SEC File No.000-55021.)
10.13	First Amendment to Lease, dated April 16, 2018, between CymaBay Therapeutics, Inc. andBMR-Pacific Research Center, LP. (Filed with the SEC as Exhibit 10.1 to our Form 10-Q, filed with the SEC on May 8, 2018, SEC File No.001-36500.)
10.14*	Offer Letter, dated December 6, 2013, between CymaBay Therapeutics, Inc. and Sujal Shah. (Filed with the SEC as Exhibit 10.24 to our Form 10-K, filed with the SEC on March 31, 2014, SEC File No.000-55021.)
10.15*	Offer Letter, dated November 21, 2013, between CymaBay Therapeutics, Inc. and Charles A. McWherter. (Filed with the SEC as Exhibit 10.26 to our Form 10-K, filed with the SEC on March 31, 2014, SEC File No.000-55021.)
10.16*	Offer Letter, dated August 2, 2017, between CymaBay Therapeutics, Inc. and Daniel Menold. (Filed with the SEC as Exhibit 10.4 to our Form 10-Q, filed with the SEC on August 10, 2017, SEC File No.001-36500.)
10.17*	Offer Letter, dated September 4, 2018, between CymaBay Therapeutics, Inc. and Klara Dickinson. (Filed with the SEC as Exhibit 10.16 to our Form 10-K, filed with the SEC on February 28, 2019, SEC File No.001-36500.)
10.18*	Offer Letter, dated August 27, 2020, between CymaBay Therapeutics, Inc. and Paul Quinlan. (Filed with the SEC as Exhibit 10.18 to our Form 10-K, filed with the SEC on March 25, 2021, SEC File No.001-35600.)
10.19*	Offer Letter, dated March 24, 2021, between CymaBay Therapeutics, Inc. and Lewis Stuart. (Filed with the SEC as Exhibit 10.1 to our Form 10-Q, filed with the SEC on August 12, 2021, SEC File No.001-35600.)
10.20*	Offer Letter, dated April 30, 2021, between CymaBay Therapeutics, Inc. and Dennis D. Kim. (Filed with the SEC as Exhibit 10.2 to our Form 10-Q, filed with the SEC on August 12, 2021, SEC File No.001-35600.)
10.21*	Non-Employee Director Compensation Program. (Filed with the SEC as Exhibit 10.17 to ourForm 10-K, filed with the SEC on February 28, 2019, SEC File No. 001-36500.)
21.1	List of subsidiaries of the Registrant.
23.1	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney. (Incorporated by reference to the signature page of this Annual Report onForm 10-K.)
31.1	Certification of President and Chief Executive Officer (Principal Executive Officer) pursuant to Rule 13-a-14(a) or Rule 15(d)-14(a) of the Exchange Act.

Exhibit No.	Description of Document
31.2	Certification of Vice President, Finance (Principal Financial Officer) pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act.
32.1	Certification of President and Chief Executive Officer (Principal Executive Officer) and Vice President, Finance (Principal Financial Officer) pursuant to 18 U.S.C. Section 1350 as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	Inline XBRL Instance Document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Document
104	Cover Page Interactive Data File (formatted as inline XBRL and contained in exhibit 101)

* Indicates management contract or compensatory plan.
# Portions of this exhibit have been omitted pursuant to a grant of confidential treatment, which portions were omitted and filed separately with the Securities and Exchange Commission.
Certain portions of this exhibit have been omitted because the omitted portions are both not material and is the type of information that CymaBay treats as private or confidential.

CymaBay Therapeutics, Inc.
Index to Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of CymaBay Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of CymaBay Therapeutics, Inc. (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the years then ended, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the years then ended, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the 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 audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

Critical audit matters are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. We determined that there are no critical audit matters.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 1994.

Redwood City, California
March 17, 2022

CymaBay Therapeutics, Inc.
Consolidated Balance Sheets
(In thousands, except share amounts and par value)

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 125,806	$ 28,193
Marketable securities	60,729	118,130
Prepaid research and development expenses	2,371	2,221
Other prepaid expenses and current assets	2,193	3,041
Total current assets	191,099	151,585
Property and equipment, net	1,178	1,761
Non-current marketable securities	8,067	—
Operating lease right-of-use asset	254	272
Other assets	1,720	207
Total assets	$ 202,318	$ 153,825
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 2,728	$ 231
Accrued research and development expenses	9,752	4,698
Other accrued liabilities	5,886	4,928
Total current liabilities	18,366	9,857
Development financing liability	50,320	—
Long-term portion of operating lease liability	695	1,262
Total liabilities	69,381	11,119
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.0001 par value: 10,000,000 shares authorized; no shares issued and outstanding	—	—
Common stock, $0.0001 par value: 200,000,000 shares authorized; 84,677,939 and 68,946,092 shares issued and outstanding as of December 31, 2021 and December 31, 2020, respectively	8	7
Additional paid-in capital	899,798	819,549
Accumulated other comprehensive (loss) income	(13)	8
Accumulated deficit	(766,856)	(676,858)
Total stockholders' equity	132,937	142,706
Total liabilities and stockholders' equity	$ 202,318	$ 153,825

See accompanying notes to the consolidated financial statements.

CymaBay Therapeutics, Inc.
Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share information)

	Year Ended December 31,	
	2021	**2020**
Operating expenses:		
Research and development	$ 64,542	$ 35,882
General and administrative	23,040	16,720
Total operating expenses	87,582	52,602
Loss from operations	(87,582)	(52,602)
Other income (expense), net:		
Interest income	167	1,616
Interest expense	(2,583)	—
Total other income (expense), net	(2,416)	1,616
Net loss	$ (89,998)	$ (50,986)
Other comprehensive loss:		
Unrealized loss on marketable securities	(21)	(72)
Total other comprehensive loss	(21)	(72)
Comprehensive loss	$ (90,019)	$ (51,058)
Basic and diluted net loss per common share	$ (1.27)	$ (0.74)
Weighted average common shares outstanding used to calculate basic and diluted net loss per common share	71,055,331	68,893,127

See accompanying notes to the consolidated financial statements.

CymaBay Therapeutics, Inc.
Consolidated Statements of Stockholders' Equity
(In thousands, except share and per share information)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balances as of December 31, 2019	68,882,459	$ 7	$812,133	$ 80	$ (625,872)	$ 186,348
Issuance of common stock upon exercise of stock options	63,633	—	92	—	—	92
Stock-based compensation expense	—	—	7,324	—	—	7,324
Net Loss	—	—	—	—	(50,986)	(50,986)
Net unrealized loss on marketable securities	—	—	—	(72)	—	(72)
Balances as of December 31, 2020	68,946,092	$ 7	$819,549	$ 8	$ (676,858)	$ 142,706
Issuance of common stock upon exercise of stock options	106,847	—	219	—	—	219
Stock-based compensation expense	—	—	9,996	—	—	9,996
Issuance of common stock and pre-funded warrants, net of $4,965 issuance costs	15,625,000	1	70,034	—	—	70,035
Net loss	—	—	—	—	(89,998)	(89,998)
Net unrealized loss on marketable securities	—	—	—	(21)	—	(21)
Balances as of December 31, 2021	84,677,939	$ 8	$899,798	$ (13)	$ (766,856)	$ 132,937

See accompanying notes to the consolidated financial statements.

CymaBay Therapeutics, Inc.
Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,	
	2021	2020
Operating activities		
Net loss	$ (89,998)	$ (50,986)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	688	632
Stock-based compensation expense	9,996	7,324
Accretion of development financing liability	2,583	—
Write-off of deferred financing costs	312	—
Net accretion and amortization of investments in marketable securities	637	(104)
Changes in assets and liabilities:		
Other prepaid expenses and current assets	386	6,716
Other assets	(1,513)	(47)
Accounts payable	2,309	(2,272)
Accrued research and development expenses	5,054	(4,520)
Other accrued liabilities	115	(1,468)
Net cash used in operating activities	(69,431)	(44,725)
Investing activities		
Purchases of property and equipment	(87)	(21)
Purchases of marketable securities	(78,084)	(176,300)
Proceeds from maturities of marketable securities	126,760	224,278
Net cash provided by investing activities	48,589	47,957
Financing activities		
Proceeds from issuance of common stock and pre-funded warrants, net of issuance costs	70,499	—
Proceeds from development financing, net of transaction costs	47,737	—
Proceeds from issuance of common stock pursuant to equity award plans	219	92
Net cash provided by financing activities	118,455	92
Net increase in cash and cash equivalents	97,613	3,324
Cash and cash equivalents at beginning of period	28,193	24,869
Cash and cash equivalents at end of period	$ 125,806	$ 28,193
Supplemental disclosure		
Cash paid for amounts included in the measurement of lease liabilities	$ 666	$ 647
Supplemental non-cash investing and financing activities		
Unpaid financing costs	$ 464	$ —

See accompanying notes to the consolidated financial statements.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Organization and Description of Business

CymaBay Therapeutics, Inc. (the Company or CymaBay) is a clinical-stage biopharmaceutical company focused on developing and providing access to innovative therapies for patients with liver and other chronic diseases with high unmet medical need. The Company's key clinical development candidate is seladelpar. Seladelpar has been primarily under development for the treatment primary biliary cholangitis (PBC), a rare liver disease. The Company was incorporated in Delaware in October 1988 as Transtech Corporation. The Company's headquarters and operations are located in Newark, California and it operates in one segment.

Liquidity

The Company has incurred net operating losses and negative cash flows from operations since its inception. During the year ended December 31, 2021, the Company incurred a net loss of $90.0 million and used $69.4 million of cash in operations. At December 31, 2021, the Company had an accumulated deficit of $766.9 million.

Historically, the Company has incurred substantial research and development expenses in the course of studying its product candidates in clinical trials. To date, none of the Company's product candidates have been approved for marketing and sale, and the Company has not recorded any revenue from product sales. Generally, the Company's ability to achieve profitability is dependent on its ability to successfully develop, acquire or in-license additional product candidates, conduct clinical trials for those product candidates, obtain regulatory approvals, and support commercialization activities for those product candidates. Any products developed will require approval of the U.S. Food and Drug Administration (FDA) or a foreign regulatory authority prior to commercial sale. The regulatory approval process is expensive, time-consuming, and uncertain, and any denial or delay of approval could have a material adverse effect on the Company. Even if approved, the Company's products may not achieve market acceptance and will face competition from both generic and branded pharmaceutical products.

During the year ended December 31, 2021, the Company completed certain financing transactions as follows:

- On July 30, 2021, the Company entered into a Development Financing Agreement (theFinancing Agreement) with ABW Cyclops SPV LP, an affiliate of Abingworth LLP (Abingworth), pursuant to which Abingworth committed to provide $75.0 million in funding in three equal quarterly installments, and an additional amount of $25.0 million at the Company's option, for a total funding commitment of up to $100 million, to support the Company's development of seladelpar for the treatment ofPBC. The Company received the first $25.0 million installment in August 2021, the second $25.0 million installment in November 2021 and the third $25.0 million installment subsequently in January 2022. For further details, refer to *Note 6—Development Financing Agreement*.
- On November 22, 2021, the Company sold 15,625,000 shares of common stock at $4.00 per share and pre-funded warrants to purchase 3,125,000 shares of common stock at $3.9999 per shares in a public equity offering, for total gross offering proceeds of approximately $75 million, before deducting approximately $5 million of underwriting discount and other offering expenses. For further details, refer to *Note 9—Stockholders' Equity.*

As of December 31, 2021, the Company had cash, cash equivalents and marketable securities totaling$194.6 million, which the Company believes is sufficient to fund its current operating plan for at least twelve months from the issuance date of its financial statements.

The Company has historically obtained, and expects to obtain in the future, additional financing to fund its business strategy throughfuture equity offerings; debt financing; one or more possible licenses, collaborations

or other similar arrangements with respect to development and/or commercialization rights of the Company's product candidates; or a combination of the above. It is unclear if or when any such transactions will occur, on satisfactory terms or at all. The Company's failure to raise capital as and when needed could have a negative impact on its financial condition and its ability to pursue its business strategies. If adequate funds are not available to the Company, it could have a material adverse effect on the Company's business, results of operations, and financial condition. Market volatility resulting from the global novel coronavirus disease (COVID-19) pandemic or other factors could also adversely impact the Company's ability to access capital when and as needed. Failure to raise sufficient capital when needed could require the Company to significantly delay, scale back or discontinue its product development programs or commercialization efforts or other aspects of its business plans, and its operating results and financial condition would be adversely affected.

2. Summary of Significant Accounting Policies

Basis of Presentation and Use of Estimates

The accompanying consolidated financial statements are comprised of the accounts of CymaBay and its wholly-owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation. The Company has no unconsolidated subsidiaries or investments accounted for under the equity method.

These consolidated statements have been prepared in accordance with accounting principles generally accepted in the United States of America (U.S. GAAP), which requires management to make informed estimates and assumptions that impact the amounts and disclosures reported in the consolidated financial statements and accompanying notes.

Accounting estimates and assumptions are inherently uncertain. Management bases its estimates on historical experience and on assumptions believed to be reasonable under the circumstances. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes, and management must select an amount that falls within that range of reasonable estimates. Actual results could differ materially from those estimates and assumptions. These estimates form the basis for making judgments about the carrying values of assets and liabilities when these values are not readily apparent from other sources. Estimates are assessed each reporting period and updated to reflect current information and any changes in estimates will generally be reflected in the period first identified.

Fair Value of Financial Instruments

The Company's financial instruments during the periods reported consist of cash, cash equivalents, marketable securities, accounts payable, certain accrued liabilities, and the development financing liability.

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 at the measurement date. Assets and liabilities that are measured at fair value are reported using a three-level fair value hierarchy that prioritizes the inputs used to measure fair value. This hierarchy maximizes the use of observable inputs and minimizes the use of unobservable inputs and is as follows:

Level 1—Quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.

Level 2—Inputs other than quoted prices in active markets that are observable for the asset or liability, either directly or indirectly.

Level 3—Inputs that are significant to the fair value measurement and are unobservable (i.e. supported by little market activity), which requires the reporting entity to develop its own valuation techniques and assumptions.

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The carrying amounts of cash, accounts payable, and certain accrued liabilities approximate their related fair values due to the short-term nature of these instruments. Cash is classified as level 1 and accounts payable and accrued liabilities as level 2 under the fair value hierarchy.

The following tables present the Company's financial assets that are measured at fair value on a recurring basis using the above input categories (in thousands):

	As of December 31, 2021			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$85,638	$ —	$ —	$ 85,638
Total cash equivalents	85,638	—	—	85,638
Marketable securities:				
U.S. and foreign commercial paper	—	28,760	—	28,760
U.S. and foreign corporate debt securities	—	23,535	—	23,535
Asset-backed securities	—	8,522	—	8,522
U.S. treasury securities	—	7,979	—	7,979
Total marketable securities	—	68,796	—	68,796
Total assets measured at fair value	$85,638	$ 68,796	$ —	$154,434

	As of December 31, 2020			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$22,415	$ —	$ —	$ 22,415
Total cash equivalents	22,415	—	—	22,415
Marketable securities:				
U.S. treasury securities	—	15,499	—	15,499
U.S. and foreign commercial paper	—	38,561	—	38,561
U.S. and foreign corporate debt securities	—	29,189	—	29,189
U.S. agency securities	—	23,994	—	23,994
Asset-backed securities	—	7,885	—	7,885
Supranational debt securities	—	3,002	—	3,002
Total marketable securities	—	118,130	—	118,130
Total assets measured at fair value	$22,415	$118,130	$ —	$140,545

The Company estimates the fair value of its money market funds, corporate debt, asset backed securities, commercial paper U.S. treasury and agency securities and supranational debt securities by taking into consideration valuations obtained from third-party pricing services. The pricing services utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker/dealer quotes on the same or similar securities, issuer credit spreads; benchmark securities; prepayment/default projections based on historical data; and other observable inputs.

The fair value of the Company's development financing liability is consistent with its carrying value, which is recorded at amortized cost. The development financing liability is classified as level 3 under the fair value hierarchy as its valuation is based on a discounted cash flow model that uses unobservable inputs such as the estimated timing of regulatory approval and attainment of certain sales milestones.

Cash, Cash Equivalents, and Marketable Securities

The Company considers all highly liquid investments with an original maturity of 90 days or less at the time of purchase to be cash equivalents. Cash and cash equivalents consist of deposits with commercial banks in checking, interest-bearing, and money market funds.

The Company invests excess cash in marketable securities with high credit ratings These securities consist primarily of corporate debt, commercial paper, asset-backed securities, U.S. treasury and agency securities and supranational debt securities and are classified as "available-for-sale." The Company considers marketable securities as short-term investments if the maturity date is less than or equal to one year from the balance sheet date. The Company considers marketable securities as long-term investments if the maturity date is in excess of one year from the balance sheet date.

Realized gains and losses from the sale of marketable securities, if any, are calculated using the specific-identification method. Realized gains and losses and declines in value judged to be other-than-temporary are included in interest income or expense in the consolidated statements of operations and comprehensive loss. Unrealized holding gains and losses are reported in accumulated other comprehensive loss in the consolidated balance sheets. To date, the Company has not recorded any impairment charges on its marketable securities related to other-than-temporary declines in market value. In determining whether a decline in market value is other-than-temporary, various factors are considered, including the cause, duration of time and severity of the impairment, any adverse changes in the investees' financial condition, and the Company's intent and ability to hold the security for a period of time sufficient to allow for an anticipated recovery in market value.

Concentration of Risk

Cash, cash equivalents, and marketable securities consist of financial instruments that potentially subject the Company to a concentration of credit risk to the extent of the fair value recorded on the balance sheet. The Company invests cash that is not required for immediate operating needs primarily in highly liquid instruments that bear minimal risk. The Company has established guidelines relating to the quality, diversification, and maturities of securities to enable the Company to manage its credit risk. The Company is exposed to credit risk in the event of a default by the financial institutions holding its cash, cash equivalents and investments and issuers of investments to the extent recorded on the consolidated balance sheets.

Certain materials and key components that the Company utilizes in its operations are obtained through single suppliers. Since the suppliers of key components and materials must be named in an NDA filed with the FDA for a product, significant delays can occur if the qualification of a new supplier is required. If delivery of material from the Company's suppliers were interrupted for any reason, the Company may be unable to supply any of its product candidates for clinical trials.

Other Risks and Uncertainties

In March 2020, the World Health Organization declared the global novel coronavirus disease (COVID-19) outbreak a pandemic. To date, the Company's operations have not been significantly impacted by the COVID-19 outbreak. However, the Company continues to monitor potential risks and uncertainties associated with operating its business during the pandemic. These risks include, but are not limited to, ongoing government advisories and restrictions on travel and workplace access, workforce shortages, and global supply chain delays, all of which could potentially impact the Company's ability to conduct its critical drug development and regulatory compliance activities. The Company cannot predict the specific extent, duration, or full impact that the COVID-19 outbreak will have on its consolidated financial condition and operations. The impact of the COVID-19 coronavirus outbreak on the financial performance of the Company will depend on future developments, including the duration and spread of the outbreak and related governmental advisories and restrictions. These developments and the impact of COVID-19 on the financial markets and the overall economy are highly uncertain. If the financial markets and/or the overall economy are impacted for an extended period, the Company's results may be adversely affected.

Property and Equipment

Property and equipment are recorded at cost, less accumulated depreciation and amortization. Depreciation and amortization are calculatedusing the straight-line method, and the costs are amortized over the estimated useful lives of the respective assets, which are generally three to seven years. Leasehold improvements are amortized over the shorter of the useful lives or the non-cancelable term of the related lease. Maintenance and repair costs are charged as expense in the consolidated statements of operations and comprehensive loss as incurred.

Long-Lived Assets

The Company reviews the carrying value long-lived assets, includingright-of-use operating lease assets, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. If a change in circumstance occurs, the Company performs a test of recoverability by comparing the carrying value of the asset or asset group to its undiscounted expected future cash flows. If cash flows cannot be separately and independently identified for a single asset, the Company will determine whether impairment has occurred for the group of assets for which the Company can identify the projected cash flows. If the carrying values are in excess of undiscounted expected future cash flows, the Company measures any impairment by comparing the fair value of the asset or asset group to its carrying value. There were no indicators of impairment of long-lived assets for any periods presented.

Leases

The Company has one lease, a non-cancelable operating lease agreement for its corporate office. The Company recognizes a lease asset for its right to use the underlying asset and a lease liability for the corresponding lease obligation. The Company determines whether an arrangement is or contains a lease at contract inception. Operating leases are included in operating lease right-of-use assets, other accrued liabilities, and long-term portion of operating lease liabilities in the Company's consolidated balance sheets at December 31, 2021 and 2020. Operating lease right-of-use assets and liabilities are recognized at the lease commencement date based on the present value of lease payments over the lease term. In determining the net present value of lease payments, the Company uses its incremental borrowing rate based on the information available at the lease commencement date. The incremental borrowing rate represents the interest rate the Company would incur at lease commencement to borrow an amount equal to the lease payments on a collateralized basis over the term of a lease. The Company considers a lease term to be the noncancelable period that it has the right to use the underlying asset, including any periods where it is reasonably assured the Company will exercise the option to extend the contract. Periods covered by an option to extend are included in the lease term if the lessor controls the exercise of that option.

The operating lease right-of-use assets also include any lease payments made and exclude lease incentives. Lease expense is recognized on a straight-line basis over the expected lease term. The Company has elected to not separate lease and non-lease components for its leased assets and accounts for all lease and non-lease components of its agreements as a single lease component. The Company does not record leases on its consolidated balance sheets when a lease has a term of one year or less.

Research and Development Expenses

Research and development expenses consist of costs incurred in identifying, developing, and testing product candidates. These expenses consist primarily of costs for research and development personnel, including related stock-based compensation; contract research organizations (CRO) and other third parties that assist in managing, monitoring, and analyzing clinical trials; investigator and site fees; laboratory services; consultants; contract manufacturing services; non-clinical studies, including materials; and allocated expenses, such as depreciation of assets, and facilities and information technology that support research and development activities. Research and

development costs are expensed as incurred, including expenses that may or may not be reimbursed under research and development funding arrangements. Payments made prior to the receipt of goods or services to be used in research and development are recorded as prepaid assets until the goods are received or services are rendered. Such payments are evaluated for current or long-term classification based on when they will be realized. Additionally, if expectations change such that the Company does not expect goods to be delivered or services to be rendered, such prepayments are charged to expense.

The Company records expenses related to clinical studies and manufacturing development activities based on its estimates of the services received and efforts expended pursuant to contracts with multiple CROs and manufacturing vendors that conduct and manage these activities on its behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows. There may be instances in which payments made to the Company's vendors will exceed the level of services provided and result in a prepayment. Payments under some of these contracts depend on factors such as the successful enrollment of subjects and the completion of clinical trial milestones. In amortizing or accruing service fees, the Company estimates the time period over which services will be performed, enrollment of subjects, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the Company's estimate, the Company will adjust the accrued or prepaid expense balance accordingly. To date, there have been no material differences from the Company's estimates to the amounts actually incurred.

Development Financing Agreement

The Company accounts for the Financing Agreement (see Note 6) as a debt instrument. Accordingly, the Company has recorded payments received under the Financing Agreement as part of a development financing liability in the Company's consolidated balance sheet. The liability is recorded at amortized cost and accreted to the contractual success fee amounts based on the estimated timing of regulatory approval and attainment of certain sales milestones using an imputed interest rate. Certain transaction fees incurred specifically to complete the Financing Agreement were capitalized and recorded as a reduction to the carrying amount of the development financing liability and are being amortized to interest expense using the effective interest rate method.

There are several factors that could affect the estimated timing of regulatory approval and attainment of sales milestones, some of which are not entirely within the Company's control. Therefore, the Company periodically reassesses the estimated timing of regulatory approval and attainment of sales milestones, and the expected contractual success fee payments due therefrom. If the timing and/or amount of such expected payments is materially different than original estimates, the Company will prospectively adjust the accretion of the development financing liability and the imputed interest rate.

The Company identified certain contingent repayment features in the Financing Agreement that are required to be bifurcated from the debt host instrument as embedded derivative liabilities; however, the Company determined the fair value of these features, both individually and in the aggregate, was immaterial at inception and as of December 31, 2021. The fair value of these features will be assessed at each reporting date and will be marked to market, if material. To determine the amount to record for the embedded derivative liabilities, the Company must assess the probability of occurrence of various potential future events that could affect the timing and/or amount of future cash flows related to the Financing Agreement.

Pre-funded Warrants

Pursuant to the Company's public equity offering completed in November2021, the Company issued pre-funded warrants to purchase 3,125,000 shares of common stock at a price of $3.9999 per share. These pre-funded warrants have an exercise price of $0.0001 per share, were fully exercisable upon issuance, and have no expiration date. The Company determined that the pre-funded warrants should be equity classified because they are freestanding financial instruments, are immediately exercisable, do not embody an obligation for the

Company to repurchase its shares, permit the holders to receive a fixed number of shares of common stock upon exercise, are indexed to the Company's common stock and meet the equity classification criteria. In addition, such pre-funded warrants do not provide any guarantee of value or return. Accordingly, the proceeds from the issuance of the warrants were recorded as additional paid-in capital on the Company's consolidated balance sheet as of December 31, 2021. Refer to *Note 9—Stockholders' Equity* for additional information.

Stock-Based Compensation

Stock-based compensation is measured at fair value on the grant date of the award. Compensation cost is recognized as expense on a straight-line basis over the vesting period for options with service conditions and forfeitures are accounted for as they occur. The Company uses the Black-Scholes option-pricing model to determine the fair value of stock option awards. The determination of fair value for stock-based awards using an option-pricing model requires management to make certain assumptions regarding subjective input variables such as expected term, dividends, volatility and risk-free rate. If actual results are not consistent with the Company's assumptions used in making these estimates, the Company may be required to increase or decrease compensation expense, which could be material to the Company's results of operations.

Income Taxes

The Company utilizes the liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between the financial reporting and the tax bases of assets and liabilities and are measured using enacted tax rates and laws that will be in effect when the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in income in the period that includes the enactment date. A valuation allowance is recorded when it is more likely than not that all or part of a deferred tax asset will not be realized. When the Company establishes or reduces the valuation allowance related to the deferred tax assets, the provision for income taxes will increase or decrease, respectively, in the period such determination is made.

The accounting guidance for uncertainty in income taxes prescribes a recognition threshold and measurement attribute criteria for the financial recognition and measurement of tax positions taken or expected to be taken in a tax return. For those benefits to be recognized, a tax position must be more likely than not to be sustained upon examination based on the technical merits of the position.

The Company is required to file federal and state income tax returns in the United States. The preparation of these income tax returns requires the Company to interpret the applicable tax laws and regulations in effect that could affect the amount of tax paid to these jurisdictions.

The Company records interest related to income tax reserves, if any, as interest expense, and any penalties would be recorded as other expense in the consolidated statements of operations and comprehensive loss.

Comprehensive Loss

Comprehensive loss includes net loss and net unrealized gains and losses on marketable securities, which are presented in a single continuous statement. Other comprehensive (loss) gain is also disclosed in the consolidated balance sheets and statements of stockholders' equity in accumulated other comprehensive income (loss), and is stated net of related tax effects, if any.

Net Loss Per Common Share

Basic net loss per share of common stock is based on the weighted average number of shares of common stock outstanding equivalents during the period. The weighted-average common shares outstanding as of

December 31, 2021 includes pre-funded warrants to purchase up to 3,125,000 shares of common stock that were issued in connection with the November 2021 public offering, as discussed in *Note 9—Stockholders' Equity*. Diluted net loss per share of common stock is calculated as the weighted average number of shares of common stock outstanding adjusted to include the assumed exercises of stock options, if dilutive. In all periods presented, the Company's outstanding stock options and incentive awards were excluded from the calculation of net loss per share because the effect would be antidilutive.

The following table sets forth the computation of basic and diluted net loss per share (in thousands, except share and per share amounts):

	Year Ended December 31,	
	2021	2020
Numerator:		
Net loss	$ (89,998)	$ (50,986)
Denominator:		
Weighted average number of common stock shares outstanding	71,055,331	68,893,127
Net loss per share	$ (1.27)	$ (0.74)

The following table shows the total outstanding securities considered anti-dilutive and therefore excluded from the computation of diluted net loss per share (in thousands):

	Year Ended December 31,	
	2021	2020
Common stock options	10,791	8,812
Incentive awards	101	101
Total	10,892	8,913

Recently Adopted Accounting Pronouncements

ASU 2019-12

In December 2019, the FASB issued ASU2019-12, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes, which removes certain exceptions to the general principles in Topic 740 related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. The new guidance also simplifies aspects of the accounting for franchise taxes and enacted changes in tax laws or rates and clarifies the accounting for transactions that result in a step-up in the tax basis of goodwill. The guidance became effective for the Company on January 1, 2021. The adoption of this standard did not have a material impact on the Company's consolidated financial statements and related disclosures for the year ended December 31, 2021.

Recently Issued Accounting Pronouncements

ASU 2016-13

In June 2016, the FASB issued ASUNo. 2016-13, Financial Instruments—Credit Losses (Topic 326):*Measurement of Credit Losses on Financial Instruments*, an amendment which modifies the measurement and recognition of credit losses for most financial assets and certain other instruments. The amendment updates the guidance for measuring and recording credit losses on financial assets measured at amortized cost by replacing the "incurred loss" model with an "expected loss" model. Accordingly, these financial assets will be presented at the net amount expected to be collected. The amendment also requires that credit losses related to

available-for-sale debt securities be recorded as an allowance through net income rather than reducing the carrying amount under the current, other-than-temporary-impairment model. In November 2019, FASB issued ASU No. 2019-10, *Financial Instruments—Credit Losses (Topic 326), Derivatives and Hedging (Topic 815) and Leases (Topic 842)*, which deferred the adoption deadline for smaller reporting companies to fiscal years beginning after December 15, 2022, including interim periods within those fiscal years. Early adoption is permitted, and entities are required to use a modified retrospective approach, with certain exceptions. The Company is currently assessing the impact of this standard on its consolidated financial statements and related disclosures.

3. Marketable Securities

Marketable available-for-sale securities consist of the following (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
As of December 31, 2021:				
Cash equivalents:				
Money market funds	$ 85,638	$ —	$ —	$ 85,638
Total cash equivalents	85,638	—	—	85,638
Current marketable securities:				
U.S. and foreign commercial paper	28,760	—	—	28,760
U.S. and foreign corporate debt securities	15,476	—	(8)	15,468
Asset-backed securities	8,524	1	(3)	8,522
U.S. treasury securities	7,982	—	(3)	7,979
Total current marketable securities	60,742	1	(14)	60,729
Non-current marketable securities:				
U.S. corporate debt securities	8,067	2	(2)	8,067
Total marketable securities	$154,447	$ 3	$ (16)	$154,434

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
As of December 31, 2020:				
Cash equivalents:				
Money market funds	$ 22,415	$ —	$ —	$ 22,415
Total cash equivalents	22,415	—	—	22,415
Current marketable securities:				
U.S. and foreign commercial paper	38,561	—	—	38,561
U.S. and foreign corporate debt securities	29,186	7	(4)	29,189
Asset-backed securities	7,883	2	—	7,885
U.S. treasury securities	23,991	3	—	23,994
U.S. agency securities	15,498	1	—	15,499
Supranational debt securities	3,003	—	(1)	3,002
Total current marketable securities	118,122	13	(5)	118,130
Total marketable securities	$140,537	$ 13	$ (5)	$140,545

The Company's commercial paper and corporate debt securities consist of U.S. and foreign securities from issuers in various sectors, including finance and industry and have similar credit quality and risk characteristics. The Company's asset-backed securities are collateralized by credit card receivables and have investment-grade

ratings. The Company's government securities are issued by the U.S. treasury and certain U.S. government-backed agencies. Supranational debt securities consist of securities issued with funding from various national governments, including the U.S.

There were no realized gains and losses for the years ended December 31, 2021 and 2020.None of these investments have been in a continuous unrealized loss position for more than 12 months as of December 31, 2021 and 2020. The Company may sell certain of its marketable securities prior to their stated maturities for reasons including, but not limited to, managing liquidity, credit risk, duration and asset allocation.

The following table shows the fair value of the Company's marketable securities, by contractual maturity, as of December 31, 2021 (in thousands):

Due less than 1 year	$ 146,367
Due between 1 and 2 years	8,067
Total fair value	$ 154,434

4. Certain Balance Sheet Items

Property and equipment consist of the following (in thousands):

	December 31,	
	2021	2020
Leasehold improvements	$ 2,429	$ 2,430
Office and computer equipment	290	290
Purchased software	44	44
Furniture and fixtures	539	451
Total	3,302	3,215
Less: Accumulated depreciation and amortization	(2,124)	(1,454)
Property and equipment, net	$ 1,178	$ 1,761

Depreciation and amortization expense for the years ended December 31, 2021 and 2020 was approximately $0.7 million and $0.6 million, respectively, and was recorded in both research and development expense and general and administrative expense in the consolidated statements of operations and comprehensive loss. All the Company's property and equipment is located in the U.S.

Other accrued liabilities consist of the following (in thousands):

	December 31,	
	2021	2020
Accrued compensation	$3,986	$3,769
Accrued professional fees and other	1,333	677
Current portion of operating lease liability	567	482
Total other accrued liabilities	$5,886	$4,928

5. License Agreement

Janssen Pharmaceutical NV and Janssen Pharmaceuticals, Inc.

In June 2006, the Company entered into an exclusive worldwide, royalty-bearing license to seladelpar and certain other PPARd compounds (the PPARd Products) with Janssen Pharmaceutical NV (Janssen NV), with the

right to grant sublicenses to third parties to make, use and sell such PPARd Products. Under the terms of the agreement, the Company has full control and responsibility over the research, development and registration of any PPARd Products and is required to use diligent efforts to conduct all such activities. Janssen NV has the sole responsibility for the preparation, filing, prosecution, maintenance of, and defense of the patents with respect to, the PPARd Products. Janssen NV has a right of first negotiation under the agreement to license PPARd Products from the Company in the event that the Company elects to seek a third-party corporate partner for the research, development, promotion, and/or commercialization of such PPARd Products. Under the terms of the agreement Janssen NV is entitled to receive up to an 8.0% royalty on net sales of PPARd Products. No amounts were incurred or accrued for this agreement as of and for the years ended December 31, 2021 and 2020.

6. Development Financing Agreement

On July 30, 2021 (the Effective Date), the Company entered into a Development Financing Agreement (the Financing Agreement) with Abingworth to provide funding to the Company to support its development of seladelpar for the treatment of primary biliary cholangitis (PBC). The Financing Agreement provides the Company up to $100.0 million in funding, of which $25.0 million was provided in August 2021, $25.0 million was provided in November 2021, and $25.0 million was provided in January 2022. The Company has an option to receive an additional $25 million (the Optional Funding) within approximately two months of enrollment completion of the Company's Phase 3 RESPONSE clinical trial. The Optional Funding is subject to certain customary funding conditions. The use of proceeds from the funding is limited to PBC "Development Program" costs incurred or paid as defined in the Financing Agreement. In return, the Company will pay to Abingworth:

(1) contingent upon the first to occur of regulatory approval of seladelpar for the treatment of PBC in the U.S., U.K., Germany, Spain, Italy or France (Regulatory Approval), fixed success payments equal to 2.0x of the funding provided, consisting of $10 million payable in 90 days after the Regulatory Approval and thereafter, payments due on the first six anniversaries of the Regulatory Approval in the amounts of $15.0 million, $22.5 million, $22.5 million, $25.0 million, $27.5 million and $27.5 million, respectively (or if the Optional Funding is provided, 133% of such payments) and

(2) variable success payments equal to 1.1x of the funding provided, consisting of sales milestone payments of (x) $17.5 million and $27.5 million, respectively (or if the Optional Funding is provided, 133% of such payments) upon first reaching certain cumulative U.S. product sales thresholds, and (y) $37.5 million (or if the Optional Funding is provided, 133% of such payment) upon first reaching a specified U.S. product sales run rate.

Promptly following receipt of Regulatory Approval, the Company is required to execute a note agreement and deliver a promissory note to Abingworth within two business days to convert the fixed and variable success payments into a note payable. At the time that Abingworth receives, collectively, an aggregate of 3.1x of the funding provided (approximately $232.5 million (or $310.0 million if the Optional Funding is provided)), the Company's payment obligations under the Financing Agreement will be fully satisfied. The Company has the option to satisfy its payment obligations to Abingworth upon Regulatory Approval, or a change of control of the Company, by paying an amount equal to the remaining payments payable to Abingworth subject to a mid-single-digit discount rate. Upon a change of control of the Company, an acceleration payment of 1.35x of the funding provided is payable, net of payments already made to Abingworth and creditable against future payments to Abingworth.

Pursuant to the Financing Agreement, the Company granted Abingworth a security interest in all its assets (other than intellectual property not related to seladelpar), provided that the Company is permitted to incur certain indebtedness. The security interest will terminate when the Company has paid Abingworth 2.0x of the funding provided or upon certain terminations of the Financing Agreement.

The Financing Agreement provides for negative, affirmative and additional covenants, which the Company must comply with for the duration of the Financing Agreement term. As of December 31, 2021, the Company was in compliance with all covenants stipulated in the Financing Agreement.

In certain instances, upon the termination of the Financing Agreement, the Company will be obligated to pay Abingworth a multiple of the amounts paid to the Company under the Financing Agreement, including specifically:

(i) 310% of such amounts in the event that Abingworth terminates the Financing Agreement due to (x) a Fundamental Breach, as defined in the Financing Agreement, (y) the bankruptcy of the Company, or (z) a safety concern resulting from gross negligence on the part of the Company or due to a safety concern that was material on the Effective Date and the material data showing such safety concern was not publicly known, disclosed to Abingworth, or in the diligence room made available to Abingworth,

(ii) 200% of such amounts in the event the Financing Agreement is terminated due to (x) Material Breach, as defined in the Financing Agreement, by the Company or (y) the security interests of Abingworth being invalidated or terminated other than as set forth in the Financing Agreement, and

(iii) 100% of such amounts in the event of certain irresolvable disagreements within the executive review committee overseeing the Company's development of seladelpar.

In addition, if, following certain terminations, the Company continues to develop seladelpar for the treatment of PBC and obtains regulatory approval, it will make the payments to Abingworth as if the Financing Agreement had not been terminated, less any payments made upon termination.

The Company shall not be obligated to make any payments to Abingworth under certain instances of technical or regulatory failure of the PBC development program as defined in the Financing Agreement.

As part of the arrangement, an executive review committee was established between the Company and Abingworth to discuss the Company's development of seladelpar.

The Company evaluated the Financing Agreement and determined it to be a research and development funding arrangement with the characteristics of a debt instrument as the transfer of financial risk to Abingworth was not considered substantive and genuine. Accordingly, the Company has recorded payments received under the Financing Agreement as part of a development financing liability in its consolidated balance sheets. The Company accounts for the overall development financing liability at amortized cost based on the estimated timing of regulatory approval and attainment of certain sales milestones and the contractual success fee payments expected to be due therefrom, as discounted using an imputed interest rate. The development financing liability will be accreted as interest expense to its expected future repayment amount over the expected life of the agreement using the effective interest rate method. Certain legal and financial advisory fees incurred specifically to complete the Financing Agreement were capitalized and recorded as a reduction to the carrying amount of the development financing liability and will also be amortized to interest expense using the effective interest method.

There are several factors that could affect the estimated timing of regulatory approval and attainment of sales milestones, some of which are not entirely within the Company's control. Therefore, the Company periodically reassesses the estimated timing of regulatory approval and attainment of sales milestones, and the expected contractual success fee payments due therefrom. If the timing and/or amount of such expected payments is materially different than original estimates, the Company will prospectively adjust the accretion of the development financing liability and the imputed interest rate.

The Company identified certain contingent repayment features in the agreement that are required to be bifurcated from the debt host instrument as embedded derivative liabilities; however, the fair value of these features was immaterial at the Effective Date and as of December 31, 2021. The fair value of the embedded derivative liabilities will be assessed at subsequent reporting dates if material.

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The following table sets forth a summary of the changes in the carrying value of the Company's development financing liability (in thousands):

Balance at December 31, 2020	$ —
Cash received	50,000
Debt discount	(2,263)
Accretion of development financing liability	2,583
Balance at December 31, 2021	$50,320

As of December 31, 2021, the development financing liability was classified as a long-term liability as the Company expects the related repayments to take place between 2024 and 2030 for purposes of the model used to calculate its carrying value. The imputed interest rate on the unamortized portion of the development financing liability was approximately 20% as of December 31, 2021.

7. Commitments and Contingencies

Indemnification

In the normal course of business, the Company enters into contracts and agreements that contain a variety of representations and warranties and provide for general indemnification, including indemnification associated with product liability or infringement of intellectual property rights. The Company's exposure under these agreements is unknown because it involves future claims that may be made against the Company that may be, but have not yet been, made. To date, the Company has not paid any claims or been required to defend any action related to these indemnification obligations, and no amounts have been accrued in the accompanying consolidated balance sheets related to these indemnification obligations.

The Company has agreed to indemnify its officers and directors for losses and costs incurred in connection with certain events or occurrences, including advancing money to cover certain costs, subject to certain limitations. The maximum potential amount of future payments the Company could be required to make under this indemnification is unlimited; however, the Company maintains insurance policies that may limit its exposure and may enable it to recover a portion of any future amounts paid. Assuming the applicability of coverage, the willingness of the insurer to assume coverage, and subject to certain retention, loss limits, and other policy provisions, the Company believes the fair value of these indemnification obligations is not material. Accordingly, the Company has not recognized any liabilities relating to these obligations as of December 31, 2021 and 2020. No assurances can be given that the covering insurers will not attempt to dispute the validity, applicability, or amount of coverage without expensive litigation against these insurers, in which case the Company may incur substantial liabilities as a result of these indemnification obligations.

Genfit Litigation

On January 15, 2021, Genfit S.A. (Genfit) filed a complaint against the Company in the U.S. District Court for the Northern District of California, alleging misappropriation of trade secrets and related causes of action based on the Company's receipt of a Genfit protocol synopsis for Genfit's Phase 3 clinical trial of its drug candidate elafibranor in patients with primary biliary cholangitis. An Amended Complaint was filed on April 16, 2021 with substantially the same allegations. Genfit seeks damages in an unspecified amount as well as injunctive relief. On March 12, 2021, the Court granted a Temporary Restraining Order (later converted to a Preliminary Injunction), prohibiting the Company from accessing or disseminating the protocol synopsis, using any Genfit trade secrets contained therein or destroying any evidence related thereto. The Company filed a Motion to Dismiss the Amended Complaint that was granted on September 9, 2021, with leave to amend. Genfit filed a Second Amended Complaint on October 15, 2021 with substantially the same allegations and claims for relief as in the original complaint. The Company filed a Motion to Dismiss most of the Second Amended Complaint that was granted on January 21, 2022, without further leave to amend. What remains in the complaint

is an alleged misappropriation of the protocol synopsis as a whole. The Company filed its Answer to what remained of the Second Amended Complaint on February 4, 2022. The Company intends to defend itself vigorously. While the outcome of any litigation is inherently uncertain, based on currently available information, management does not currently believe a loss associated with this matter is probable, nor is any amount reasonably estimable, and accordingly no amounts have been recorded or disclosed.

8. Leases

The Company has one operating lease pertaining to 17,698 square feet of corporate office space in Newark, California pursuant to a lease agreement that commenced January 16, 2014 and was amended on April 16, 2018. At December 31, 2021 and December 31, 2020, the Company's lease portfolio had a weighted average remaining term of 2.1 years, and 3.1 years, respectively, with an option to extend for an additional 5 years. The lease requires monthly lease payments that are subject to annual increases throughout the lease term. The optional period has not been considered in the determination of the right-of-use assets or lease liabilities associated with this lease as the Company did not consider it reasonably certain it would exercise the option.

The Company cannot determine the implicit rate in its lease, and therefore the Company uses its incremental borrowing rate as the discount rate when measuring operating lease liabilities. The incremental borrowing rate represents an estimate of the interest rate the Company would incur at lease commencement to borrow an amount equal to the lease payments on a collateralized basis over the term of a lease within a particular currency environment. The Company used an incremental borrowing rate as of the date of adoption for leases that commenced prior to January 1, 2019.

For the years ended December 31, 2021 and 2020, the Company incurred $0.6 million and $0.5 million, respectively, of lease costs included in operating expenses in the consolidated statements of operations and comprehensive loss in relation to its operating lease, a portion of which was variable rent expense and not included within the measurement of the Company's operating ROU assets and lease liabilities. The variable rent expense consists primarily of the Company's proportionate share of operating expenses, property taxes, and insurance and is classified as lease expense due to the Company's election to not separate lease and non-lease components. Short-term lease costs were not material. At December 31, 2021 and December 31, 2020, the Company's operating lease right-of-use asset totaled $0.3 million and $0.3 million, respectively, and the operating lease liability totaled $1.3 million and $1.7 million, respectively. As of December 31, 2021, the short-term portion of the operating lease liability was $0.6 million and is contained within other accrued liabilities on the balance sheet, with the remaining $0.7 million liability reported on the balance sheet as long-term portion of operating lease liability.

As of December 31, 2021, the maturities of the Company's operating lease liabilities were as follows (in thousands):

Year ending December 31,	
2022	$ 686
2023	707
2024	30
Total undiscounted future minimum lease payments	1,423
Less imputed interest	161
Total operating lease liability	1,262
Less: current portion of operating lease liability	567
Long-term portion of lease liability	$ 695

9. Stockholders' Equity

Preferred and Common Stock Authorized

The Company is authorized to issue 10,000,000 shares of preferred stock as of December 31, 2021 and 2020, and200,000,000 shares of common stock as of December 31, 2021 and 2020.

Common Stock Reserved for Future Issuance

As of December 31, 2021 and 2020, the Company had reserved shares of common stock for future issuances as follows:

	December 31,	
	2021	2020
Prefunded warrants to purchase common stock	3,125,000	—
Equity award plans:		
Options and incentive awards outstanding, all equity plans	10,892,613	8,913,071
Equity awards available for future grant—2013 Plan	1,588,613	167,159
Equity awards available for future grant—2020 Plan	—	750,000
Total shares of common stock reserved for future issuance	15,606,226	9,830,230

Sale of Common Stock and Prefunded Warrants

On November 22, 2021, pursuant to a shelf registration statement on FormS-3, the Company issued 15,625,000 shares of its common stock at $4.00 per share in an underwritten public offering. Concurrently, the Company sold to certain existing investors who did not participate in the common stock sale pre-funded warrants to purchase up to an aggregate of3,125,000 shares of common stock at a purchase price of $3.9999 per pre-funded warrant, which represents the per share public offering price for the common stock less the $0.0001 per share exercise price for each pre-funded warrant. The aggregate net proceeds to the Company from this offering was $70.5 million, after deducting underwriting discounts and commissions and other offering expenses. The underwriters also were granted a 30-day option to purchase an additional2,812,500 shares of common stock at the public offering price per share less underwriting discounts and commissions. This option was not exercised, and it expired on December 22, 2021.

The pre-funded warrants do not expire and are immediately exercisable at any time by either (i) payment in full in immediately available funds for the number of shares of common stock purchased upon such exercise or (ii) a cashless exercise in the event of certain fundamental transactions, in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the pre-funded warrant. A holder will not be entitled to exercise any portion of anypre-funded warrant if the holder's ownership of the Company's common stock would exceed 4.99% to 14.99% following such exercise.

In the event of certain fundamental transactions, the holders of thepre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction without regard to any limitations on exercise contained in the pre-funded warrants.

The pre-funded warrants were determined to be equity classified; accordingly, proceeds received from their issuance were recorded as a component of stockholders' equity within additional paid-in capital. None of the pre-funded warrants were exercised in 2021 and therefore remain outstanding as of December 31, 2021.

At-the-Market (ATM) Facility

In July 2020, the Company filed a $200.0 million registration statement on Form S-3 with the SEC and entered into an at-the-market facility (ATM) to sell up to $75.0 million of common stock under the registration statement. To date, the Company has not sold any shares of common stock under the ATM.

10. Stock Plans and Stock-Based Compensation

Stock Plans

In September 2013, the Company's stockholders approved the 2013 Equity Incentive Plan (the 2013 Plan), under which shares of common stock are reserved for the granting of incentive stock options, nonqualified stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance stock awards, performance cash awards and other stock awards by the Company. These awards may be granted to employees, members of the Board of Directors, and consultants. The 2013 Plan has a term of ten years and replaced the 2003 Equity Incentive Plan, which had similar terms. The 2013 Plan permits the Company to (i) grant incentive stock options to directors and employees at not less than 100% of the fair value of common stock on the date of grant; (ii) grant nonqualified options to employees, directors, and consultants at not less than 85% of fair value; (iii) award stock bonuses; and (iv) grant rights to acquire restricted stock at not less than 85% of fair value. Options generally vest over a four year period and have a term of ten years. Options granted to 10% stockholders have a maximum term of five years and require an exercise price equal to at least 110% of the fair value on the date of grant. The exercise price of all options granted to date has been at least equal to the fair value of common stock on the date of grant. Stock option exercises are settled with shares reserved under the 2013 Plan. The share reserve under the 2013 Plan will automatically increase on January 1st of each year, for a period of not more than ten years, in an amount equal to 5% of the total number of shares of capital stock outstanding on December 31st of the preceding calendar year, unless the Board determines otherwise prior to December 31st of such calendar year.

In October 2020, the Company's board of directors approved the 2020 New Hire Plan (the 2020 Plan), under which shares of common stock are reserved for the granting of nonqualified stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance stock awards, performance cash awards and other stock awards by the Company as an inducement to prospective new hire employees of the Company. The 2020 Plan has a term of ten years. The 2020 Plan permits the Company to (i) grant nonqualified options to new hire employees at not less than 85% of fair value; (ii) award stock bonuses; and (iii) grant rights to acquire restricted stock at not less than 85% of fair value. Options generally vest over a four year period and have a term of ten years. The share reserve under the 2020 Plan may be increased at the discretion of and approval by the board of directors.

Stock Plan Activity

As of December 31, 2021, there were 1,588,613 and no shares available for grant under the 2013 and 2020 Plans, respectively. On January 1, 2022, in accordance with the annual share increase provision in the 2013 Plan, the Company added 4,233,896 shares to the 2013 Plan share reserve.

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

	Shares Subject to Outstanding Options	Weighted-Average Exercise Price of Options	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2020	8,811,630	$ 6.35		
Options granted	2,660,965	4.84		
Options exercised	(106,847)	2.05		
Options forfeited	(307,018)	5.89		
Options expired	(267,299)	7.60		
Outstanding as of December 31, 2021	10,791,431	$ 6.01	7.28	$ 1,514
Vested and expected to vest as of December 31, 2021	10,791,431	$ 6.01	7.28	$ 1,514
Exercisable as of December 31, 2021	6,327,680	$ 6.62	6.22	$ 1,510

The total intrinsic value of options exercised was $0.2 million and $0.4 million for the years ended December 31, 2021 and 2020, respectively.

The total fair value of options vested was $0.7 million and $3.3 million for the years ended December 31, 2021 and 2020, respectively.

As of December 31, 2021, unamortized stock-based compensation expense of $16.9 million is expected to be recognized over a weighted average period of 2.6 years.

Incentive Awards

In December 2013, January 2014, and April 2014, as permitted by the 2013 Plan, the Company issued certain incentive awards to directors, employees and a consultant which are subject to 252,752 shares of the Company's common stock and are exercisable at a weighted average price of $5.21 per share when vested. The Company may determine at its option whether to settle exercised awards in shares of common stock or in cash. Each recipient's incentive award defines the number of common shares that may be acquired upon exercise provided the Company chooses to settle in shares. For awards settled in cash, the Company must pay the recipient the excess of the fair market value of the Company's common stock on the date of exercise over the exercise price paid by the recipient multiplied by the number of shares the recipient would be entitled to receive had the award been settled in shares of the Company's common stock.

Pursuant to their terms, the incentive awards have a term of 10 years and were initially scheduled to vest 100% on the second anniversary of their grant date. However, as a result of the approval by the Company's stockholders of a 500,000 share increase to the 2013 Plan's share reserve in June 2014, the incentive awards were automatically modified to vest monthly over four years effective from their grant date The Company recognized the value of the incentive awards over the remaining four year vesting period which ended in the first quarter of 2018.

The Company recorded no stock-based compensation expense in the years ended December 31, 2021 and 2020 pertaining to its incentive awards. Incentive awards outstanding totaled 101,182 and 101,441 as of December 31, 2021 and 2020, respectively.

Stock-Based Compensation Expense

Stock-based compensation expense is included in the consolidated statements of operations and comprehensive loss and is as follows (in thousands):

	Year Ended December 31,	
	2021	2020
Research and development	$4,470	$2,739
General and administrative	5,526	4,585
Total stock-based compensation expense	$9,996	$7,324

Valuation Assumptions

The following table presents the weighted-average assumptions the Company used in the Black-Scholes option-pricing model to derive the grant date fair values of stock options granted in each of the years presented along with the resulting estimated weighted-average grant date fair values per share:

	Year Ended December 31,	
	2021	2020
Expected term (years)	6.1	6.1
Expected volatility	104%	105%
Risk-free interest rate	0.9%	0.4%
Expected dividend yield	—	—
Weighted-average grant date fair value per share	$3.91	$3.91

Expected Term

The Company does not believe it can currently place reliance on its historical exercise and post-vesting termination activity to provide accurate data for estimating the expected term. Therefore, for stock option grants made during the years ended December 31, 2021 and 2020, the Company has elected to use the simplified method for estimating the expected term, which is an average of the contractual term of the options and its ordinary vesting period. The expected term represents the period of time that options are expected to be outstanding.

Expected Volatility

The Company estimates expected volatility by measuring the historical volatility of its common stock price over a historical period commensurate with the expected term of the related award.

Risk-Free Interest Rate

The risk-free interest rate assumption was based on U.S. treasury instruments with constant maturities whose term was consistent with the expected term of stock options granted by the Company.

Expected Dividend Yield

The Company has never declared or paid cash dividends and does not plan to pay cash dividends in the foreseeable future. Consequently, the Company uses an expected dividend yield of zero.

11. 401(k) Plan

The Company provides a qualified 401(k) savings plan for its employees. All employees are eligible to participate, provided they meet the requirements of the plan. As is permitted under the plan, the Company has elected to match employee contributions up to $750 and accordingly matching contributions totaling an insignificant amount were made in the years ended December 31, 2021 and 2020.

12. Income Taxes

No provision for U.S. income taxes exists due to tax losses incurred in all periods presented. All losses incurred were U.S. basedSignificant components of the Company's deferred tax assets are as follows (in thousands):

	December 31,	
	2021	2020
Deferred tax assets:		
Federal and state net operating loss carryforwards	$ 129,898	$ 123,144
State and federal research and development tax credit carryforwards	31,951	28,861
Capitalized research and development	5,670	2,363
Stock-based compensation	5,329	3,822
Other	1,222	1,256
Total deferred tax assets	174,070	159,446
Deferred tax liabilities:		
Depreciation and amortization	(158)	(269)
Other	(53)	(57)
Total deferred tax liabilities	(211)	(326)
Valuation allowance	(173,859)	(159,120)
Net deferred tax assets	$ —	$ —

Realization of the net deferred tax assets is dependent upon future taxable income, if any, the amount and timing of which is uncertain. Based on the weight of available positive and negative objective evidence, management believes it more likely than not that the Company's deferred tax assets are not realizable. Accordingly, the net deferred tax assets have been fully offset by a valuation allowance. The net valuation allowance increased by $14.7 million and $17.2 million due to the increase in the Company's taxable losses during the years ended December 31, 2021 and 2020, respectively.

The following is a reconciliation of the expected statutory federal income tax provision to the actual income tax provision (in thousands):

	December 31,	
	2021	2020
Income tax benefit at federal statutory tax rate	$(18,900)	$(10,707)
Change in valuation allowance	14,739	17,181
State income taxes, net of federal benefit	(267)	(4,768)
Research credits	(2,802)	(2,911)
Cancelled options	141	982
Development financing liability	6,654	—
Permanent differences	429	152
Other, net	6	71
Income tax (benefit) expense	$ —	$ —

Pursuant to Internal Revenue Code (IRC), Section 382 and 383, use of the Company's U.S. federal and state net operating loss and research and credit carryforwards may be limited in the event of a cumulative change in ownership of more than 50.0% within a three-year period. The Company completed an analysis under IRC Sections 382 and 383 through December 21, 2007 and determined that the Company's net operating losses and research and development credits were subject to limitations due to changes in ownership through December 31, 2007. The net operating loss carryforwards reflected in the deferred tax assets at December 31, 2021 have been adjusted to reflect Section 382 limitations resulting from that change. The Company has been in a net operating loss position since 2008. The Company has not performed any additional analysis for IRC Sections 382 and 383 and there is a risk that additional changes in ownership could have occurred since December 31, 2007. If a change in ownership were to have occurred, additional net operating loss and tax credit carryforwards could be eliminated or restricted. If eliminated, the related asset would be removed from the deferred tax asset schedule with a corresponding reduction in the valuation allowance.

As of December 31, 2021, the Company had federal net operating loss carryforwards of $522.7 million and state net operating loss carryforwards of $288.3 million to offset future taxable income, if any. In addition, the Company had federal research and development tax credit carryforwards of $10.2 million, federal orphan drug tax credit carryforwards of $24.8 million, and state research and development tax credit carryforwards of $6.2 million. If not utilized, the federal net operating losses for the years beginning before January 1, 2018 of $255.7 million will expire beginning in 2024 through 2037, and the federal net operating losses for the tax years beginning after January 1, 2018 of $267.0 million will be carried forward indefinitely (subject to certain utilization limitations). The state net operating loss carryforwards will expire beginning in 2028 through 2041. The federal research and development and federal orphan drug tax credit carryforwards expire 2021 through 2041, and the state tax credit will carry forward indefinitely. Interest and penalties for the years ended December 31, 2021 and 2020 were not material. The following table summarizes activity related to the Company's gross unrecognized tax benefits (in thousands):

	Total
Balances as of December 31, 2019	6,386
Decreases related to prior year tax positions	(58)
Increases related to 2020 tax positions	877
Balances as of December 31, 2020	$7,205
Increases related to prior year tax positions	9
Increases related to 2021 tax positions	783
Balances as of December 31, 2021	$7,997

The unrecognized tax benefits, if recognized, would not have an impact on the Company's effective tax rate assuming the Company continues to maintain a full valuation allowance position. Based on prior year's operations and experience, the Company does not expect a significant change to its unrecognized tax benefits over the next twelve months. The unrecognized tax benefits may increase or change during the next year for unexpected or unusual items for items that arise in the ordinary course of business.

The Company files income tax returns in the U.S. federal and California jurisdictions and is not currently under examination by federal, state, or local taxing authorities for any open tax years. Due to net operating loss carryforwards, the tax years 2001 to 2021 remain open for income tax examination by tax authorities in the U.S. and states in which the Company files tax returns.

In March 2020, the Families First Coronavirus Response Act (FFCR Act) and the Coronavirus Aid, Relief, and Economic Security Act (CARES Act) were each enacted in response to the COVID-19 pandemic. The FFCR Act and the CARES Act contain numerous income tax provisions relating to refundable payroll tax credits, deferment of employer side social security payments, net operating loss carryback periods, alternative minimum

tax credit refunds, modifications to the net interest deduction limitations and technical corrections to tax depreciation methods for qualified improvement property.

In June 2020, Assembly Bill 85 (A.B. 85) was signed into California law. A.B. 85 provides for a three-year suspension of the use of net operating losses for medium and large businesses and a three-year cap on the use of business incentive tax credits to offset no more than $5.0 million of tax per year. A.B. 85 suspends the use of net operating losses for taxable years 2020, 2021 and 2022 for certain taxpayers with taxable income of $1.0 million or more. The carryover period for any net operating losses that are suspended under this provision will be extended. A.B. 85 also requires that business incentive tax credits including carryovers may not reduce the applicable tax by more than $5.0 million for taxable years 2020, 2021 and 2022.

In December 2020, the Consolidated Appropriations Act, 2021 (CAA) was signed into law. The CAA included additional funding through tax credits as part of its economic package for 2021.

The FFCR Act, CARES Act, A.B. 85 and CAA did not have a material impact on the Company's consolidated financial statements; however, the Company continues to examine the impacts the FFCR Act, CARES Act, A.B. 85 and CAA may have on its business, results of operations, financial condition and liquidity.

Item 16. Form 10-K Summary

None.

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SIGNATURES

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

CymaBay Therapeutics, Inc.
Registrant

March 17, 2022
Date

/s/ Sujal Shah
Sujal Shah
President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Sujal Shah and Daniel Menold, as his or her true and lawful attorney-in-fact and agent, with full power of substitution for him or her, and in his or her name in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, and any of them or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1934, this report has been signed by the following persons on behalf of the Registrant in the capacities indicated on the date set forth below:

Name and Signature	Title	Date
/s/ Sujal Shah Sujal Shah	President, Chief Executive Officer and Director *(Principal Executive Officer)*	March 17, 2022
/s/ Daniel Menold Daniel Menold	Vice President, Finance *(Principal Financial and Accounting Officer)*	March 17, 2022
/s/ Robert J. Wills Robert J. Wills, Ph.D.	Director	March 17, 2022
/s/ Kurt von Emster Kurt von Emster, CFA	Director	March 17, 2022
/s/ Caroline Loewy Caroline Loewy	Director	March 17, 2022
/s/ Thomas G. Wiggans Thomas G. Wiggans	Director	March 17, 2022
/s/ Janet Dorling Janet Dorling	Director	March 17, 2022

Exhibit 21.1

List of Subsidiaries

Name of Subsidiary	State or Jurisdiction in Which Incorporated or Organized
CymaBay UK, Ltd.	United Kingdom
CymaBay Ireland, Limited	Ireland
CymaBay Canada, Ltd.	Canada

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

(1) Registration Statement (Form S-3 No. 333-239670) of CymaBay Therapeutics, Inc., and

(2) Registration Statements (Form S-8 Nos. 333-195211, 333-198289, 333-202941, 333-210453, 333-216905, 333-223687, 333-226741, 333-229953, and 333-254697) pertaining to the Metabolex, Inc. 2003 Equity Incentive Plan, the CymaBay Therapeutics, Inc. 2013 Equity Incentive Plan, and the CymaBay Therapeutics, Inc.2020 New Hire Plan;

of our report dated March 17, 2022, with respect to the consolidated financial statements of CymaBay Therapeutics, Inc. included in this Annual Report (Form 10-K) of CymaBay Therapeutics, Inc. for the year ended December 31, 2021.

/s/ Ernst & Young LLP

Redwood City, California
March 17, 2022

Exhibit 31.1

CERTIFICATIONS

I, Sujal Shah, certify that:

1. I have reviewed this Form 10-K of CymaBay Therapeutics, Inc.;

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

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

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

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

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

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

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

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

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

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

Date: March 17, 2022

/s/ Sujal Shah
Sujal Shah
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Daniel Menold, certify that:

1. I have reviewed this Form 10-K of CymaBay Therapeutics, Inc.;

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

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

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

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

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

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

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

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

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

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

Date: March 17, 2022

/s/ Daniel Menold
Daniel Menold
Vice President, Finance
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Sujal Shah., President and Chief Executive Officer and Daniel Menold, Vice President, Finance of CymaBay Therapeutics, Inc. (the "Company"), hereby certifies that, to the best of his knowledge:

1. The Company's Annual Report on Form 10-K for the period ended December 31, 2021, to which this Certification is attached as Exhibit 32.1 (the "Annual Report") fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act, and

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

In **Witness Whereof**, the undersigned have set their hands hereto as of the 17th day of March, 2022.

/s/ Sujal Shah
Sujal Shah
President and Chief Executive Officer
(Principal Executive Officer)

/s/ Daniel Menold
Daniel Menold
Vice President, Finance
(Principal Financial and Accounting Officer)

This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of CymaBay Therapeutics, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.