

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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2020

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO

Commission File Number 001-38981

Mirum Pharmaceuticals, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware

(State or other jurisdiction of
incorporation or organization)

950 Tower Lane, Suite 1050, Foster City, California

(Address of principal executive offices)

83-1281555

(I.R.S. Employer
Identification No.)

94404

(Zip Code)

Registrant's telephone number, including area code: (650) 667-4085

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value \$0.0001 per share	MIRM	Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES NO

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES NO

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
Emerging growth company	<input checked="" type="checkbox"/>		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES NO

The aggregate market value of the Registrant's common stock held by non-affiliates of the Registrant as of June 30, 2020, the last business day of the Registrant's most recently completed second fiscal quarter, was approximately \$243.5 million, based on the closing price of the Registrant's common stock on the Nasdaq Global Market of \$19.46 per share.

The number of shares of Registrant's common stock, par value \$0.0001 per share, outstanding as of March 5, 2021 was 30,419,707.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's definitive proxy statement for its 2021 Annual Meeting of Stockholders, which the Registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the Registrant's fiscal year ended December 31, 2020, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (the “Annual Report”) may contain “forward-looking statements” within the meaning of the federal securities laws made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth under Part I, Item 1A, “Risk Factors” in this Annual Report. Except as required by law, we assume no obligation to update these forward-looking statements, whether as a result of new information, future events or otherwise. These statements, which represent our current expectations or beliefs concerning various future events, may contain words such as “may,” “will,” “expect,” “anticipate,” “intend,” “plan,” “believe,” “estimate” or other words indicating future results, though not all forward-looking statements necessarily contain these identifying words. Such statements may include, but are not limited to, statements concerning the following:

- our ability to obtain and maintain regulatory approval for our product candidates or any of our future product candidates, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- the commercialization of our product candidates, if approved;
- our ability to develop and maintain sales and marketing capabilities, whether alone or with potential future collaborators;
- our plans to research, develop and commercialize our product candidates, including the timing of our ongoing clinical trials of maralixibat and volixibat;
- our expectations regarding the size of target patient populations for our product candidates, if approved for commercial use, and any additional product candidates we may develop;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates, as well as third-party payor coverage and reimbursement for our product candidates;
- our ability to attract collaborators with development, regulatory and commercialization expertise;
- our expectations regarding our ability to obtain, maintain, enforce and defend our intellectual property protection for our product candidates;
- regulatory and legal developments in the United States and foreign countries;
- the performance of our third-party suppliers and manufacturers;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- our estimates regarding the impact of the ongoing COVID-19 pandemic on our business and operations, the business and operations of our collaborators and on the global economy;
- our ability to obtain funding for our operations; and
- the accuracy of our estimates regarding expenses, capital requirements and needs for additional financing.

Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. You should be aware that the occurrence of any of the events discussed under Part I, Item 1A, "Risk Factors" and elsewhere in this Annual Report could substantially harm our business, results of operations and financial condition and that if any of these events occurs, the trading price of our common stock could decline and you could lose all or a part of the value of your shares of our common stock.

The cautionary statements made in this Annual Report are intended to be applicable to all related forward-looking statements wherever they may appear in this Annual Report. We urge you not to place undue reliance on these forward-looking statements, which speak only as of the date of this Annual Report. Except as required by law, we assume no obligation to update our forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in any forward-looking statements, whether as a result of new information, future events or otherwise.

SUMMARY OF RISKS ASSOCIATED WITH OUR BUSINESS

An investment in shares of our common stock involves a high degree of risk. Below is a list of the more significant risks associated with our business. This summary does not address all of the risks that we face. Additional discussion of the risks listed in this summary, as well as other risks that we face, are set forth under Part I, Item 1A, "Risk Factors" in this Annual Report.

- We have a very limited operating history, and we have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.
- Our business is dependent on the success of our product candidates, each of which require significant clinical testing before we can seek regulatory approval and potentially launch commercial sales.
- We have encountered and may continue to encounter delays and difficulties enrolling patients in our clinical trials, and as a result, our clinical development activities could be delayed or otherwise adversely affected.
- Our product candidates are subject to extensive regulation and compliance, which is costly and time consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates.
- Our clinical trials may fail to adequately demonstrate the safety and efficacy of our product candidates, which could prevent or delay regulatory approval and commercialization.
- Clinical drug development involves a lengthy and expensive process with uncertain outcomes, and results of earlier studies and trials may not be predictive of future trial results.
- Any delays in the commencement or completion, or termination or suspension, of our clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.
- Our applications for marketing authorization with regulatory authorities may not be accepted or may require additional studies or manufacturing requirements to be completed before marketing authorization is granted.
- Even if we obtain regulatory approval for our product candidates, our product candidates may not gain market acceptance among physicians, patients, tertiary care centers, transplant centers and others in the medical community.
- We currently have a limited marketing and sales organization and as a company, we have never commercialized a product before. If we are unable to adequately establish marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, we may not be able to generate viable product revenues. Even if we adequately establish such capabilities, market acceptance or reimbursement of our products may be lower than expected.
- We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.
- We will need substantial additional financing to develop our product candidates and implement our operating plans. If we fail to obtain additional financing, we may be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- We depend on intellectual property licensed from third parties and termination of any of these licenses could result in the loss of significant rights, which would harm our business.
- If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, or if the scope of the intellectual property protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our product candidates, if approved, may be adversely affected.

Item 1. Business.**Overview**

We are a biopharmaceutical company focused on the development and commercialization of a late-stage pipeline of novel therapies for debilitating liver diseases. We focus on diseases for which the unmet medical need is high and the biology for treatment is clear. Our pipeline consists of two clinical-stage product candidates with mechanisms of action that have potential utility across a wide range of orphan cholestatic liver diseases. Cholestasis is characterized by impaired flow of bile resulting in accumulation of toxic bile acids both in the liver and systemically. This can lead to severe pruritus, or itching, high symptomatic burden, liver injury, progressive liver disease and, if left untreated, can result in fibrosis, cirrhosis, liver failure and death. Most cholestatic liver diseases have no approved medicines and often the only option is to resort to liver transplant to address the related symptoms and progressive liver disease.

We are developing maralixibat for the treatment of pediatric patients with Alagille syndrome (“ALGS”), progressive familial intrahepatic cholestasis (“PFIC”) and biliary atresia (“BA”). Across all three settings, the majority of diagnosed children are estimated to receive a liver transplant before adulthood. In particular, in patients with ALGS and PFIC, the severe pruritus can be the leading driver for a transplant. In the third quarter of 2020, we initiated a rolling submission of a New Drug Application (“NDA”), for the treatment of cholestatic pruritus in patients with ALGS to the U.S. Food and Drug Administration (“FDA”) and subsequently completed our NDA submission in January 2021. We are planning for a potential launch in ALGS in the second half of 2021. We have also submitted a marketing authorization application (“MAA”) to the European Medicines Agency (“EMA”) for maralixibat for the treatment of PFIC2, which has been accepted for review. In parallel, we are also conducting the Phase 3 MARCH clinical trial in PFIC evaluating higher doses of maralixibat in a broader population of PFIC subtypes, for which we expect to complete enrollment in the second quarter of 2021 and announce topline data in early 2022. Additionally, we have initiated recruitment for the EMBARK Phase 2 clinical trial for BA.

We are developing volixibat for the treatment of adult patients with cholestatic liver diseases, including primary sclerosing cholangitis (“PSC”), intrahepatic cholestasis of pregnancy (“ICP”) and primary biliary cholangitis (“PBC”). PSC and PBC are progressive immuno-inflammatory driven cholestatic conditions that cause debilitating pruritus and progressive liver damage related to disruption in bile acid transit. ICP is a cholestatic liver disorder which occurs during pregnancy that results in high symptomatic burden for the mother and can be fatal for the fetus. In all of these indications, we believe the elevated bile acid pool drives symptomatic burden and life-threatening progression and ASBT inhibition has the potential to reduce these elevated bile acid levels. We dosed the first patient in the VISTAS Phase 2b clinical trial of volixibat in PSC in January 2021, and we have initiated recruitment for the OHANA clinical trial of volixibat in ICP. We expect to dose the first patient in the clinical trial of volixibat in PBC in the second half of 2021. We believe we have incorporated material regulatory feedback for these three studies such that, if successful, their results may support filing for regulatory approval for their respective indications.

Our Product Pipeline

Our team has strategically assembled a pipeline of novel product candidates that target a specific biological mechanism implicated in cholestatic liver diseases. We own exclusive worldwide rights to each of our product candidates. Maralixibat and volixibat are investigational, novel, oral, minimally-absorbed agents designed to inhibit the apical sodium-dependent bile acid transporter (“ASBT”), which is primarily responsible for recycling bile acids from the intestine to the liver. The following graphic depicts each of our product candidates, the respective indications we are pursuing, the expected next milestones and regulatory designations:

	Phase 1	Randomized Studies	Filing	Marketing Authorization
Maralixibat				
Atagille Syndrome (ALGS)				
<i>BTD for pruritus associated with ALGS (FDA)</i> <i>Rare Pediatric Disease (FDA); Orphan (FDA/EMA)</i>			Expanded Access Program launched	
Progressive Familial Intrahepatic Cholestasis (PFIC)				
<i>BTD for PFIC2 (FDA)</i> <i>Rare Pediatric Disease (FDA); Orphan (FDA/EMA)</i>			US	EU
Biliary Atresia (BA)				
<i>Orphan (FDA/EMA)</i>			Enrolling	
Volixibat				
Primary Sclerosing Cholangitis (PSC)				
			Enrolling	
Intrahepatic Cholestasis of Pregnancy (ICP)				
			Enrolling	
Primary Biliary Cholangitis (PBC)				
			Planning (FPI: H2 2021)	

Abbreviations: FPI, First Patient In; BTD, Breakthrough Therapy Designation; FDA, U.S. Food and Drug Administration; EMA, European Medicines Agency

Maralixibat

Our lead product candidate, maralixibat, is a novel, oral, minimally-absorbed agent designed to selectively inhibit ASBT, also known as ileal bile acid transporter (“IBAT”). ASBT is primarily responsible for recycling bile acids from the intestine back to the liver. ASBT inhibition results in more bile acids being excreted in the feces, leading to lower levels of bile acids systemically, thereby reducing bile acid mediated effects and liver damage. We believe that by targeting bile acids in these settings, maralixibat has the potential to improve long-term outcomes and symptoms in our targeted settings and provide an alternative treatment to liver transplant. Maralixibat possesses an extensive safety dataset, having been evaluated in more than 1,600 human subjects. Maralixibat has been studied in a number of completed and ongoing clinical trials in ALGS and PFIC with over 120 children treated and some on study for over seven years. We received breakthrough therapy designation for maralixibat for the treatment of pruritus associated with ALGS in patients one year of age and older and for the treatment of PFIC2. We also have orphan designation for ALGS, PFIC and BA, and rare pediatric disease designation granted for ALGS and PFIC.

Maralixibat in ALGS

ALGS is a multi-organ disease that affects approximately one in 30,000 births in the United States and Europe, and patients typically present in infancy or early childhood. Based on primary market research we believe that in the United States there are approximately 2,000 to 2,500 children with ALGS who are eligible for treatment with maralixibat. There are no approved therapies for the treatment of ALGS. Partial External Biliary Diversion (“PEBD”) surgery is associated with significant complications, and liver transplantation is the only definitive treatment for cholestasis due to ALGS, but is expensive, requires long-term administration of immuno-suppressants, and only a portion of the patients who require a liver transplant are able to match with a suitable donor organ or can tolerate the surgery.

In ICONIC, a Phase 2b placebo-controlled randomized drug withdrawal clinical trial, there was a clinically and statistically significant difference in pruritus between the treatment group and placebo group as measured by ItchRO(Obs) score ($p < 0.0001$). The ItchRO(Obs) score is a caregiver-reported outcome assessment developed for use in cholestatic liver diseases, which measures severity of itch on a 0-4 scale. Additionally, at week 48 as compared to baseline, 72% of patients had a clinically meaningful reduction in the ItchRO(Obs) score ($p < 0.0001$); mean serum bile acids (“sBA”) were reduced by 36% ($p < 0.01$); xanthomas, which are deposits of cholesterol under the skin, were decreased by 44% ($p < 0.01$), as measured by the Clinician Xanthoma Scale; and quality of life scores improved by a mean of 9.5 points. Maralixibat has been granted orphan drug designation for ALGS by the FDA and EMA and breakthrough designation for the treatment of pruritus associated with ALGS in patients one year of age

and older by the FDA. Further, long-term analysis of the ICONIC clinical trial has shown durable response in sBA, pruritus, xanthomas and growth in patients remaining on study at week 191.

We have completed our NDA submission for maralixibat for the treatment of cholestatic pruritus in patients with ALGS. If our application is accepted for filing by the FDA, we expect a review decision in the second half of 2021 and, as a result, are preparing for a potential commercial launch of maralixibat in this indication in the United States.

Maralixibat in PFIC

PFIC affects approximately one in 50,000 to 100,000 births in the United States and Europe and typically presents within the first three to six months of life. Currently, there are no approved therapies for the treatment of PFIC. Surgical options such as PEBD and liver transplantation can be effective, but are expensive, may require life-long administration of immuno-suppressants and have potential for significant comorbidities. Only a portion of the patients who require a liver transplant are able to match with a suitable donor organ, and there can be serious complications, for example, rapid re-occurrence of disease and steatosis.

We have submitted an MAA for maralixibat for the treatment of PFIC2 with the EMA which is currently under review. This submission is based on five-year results from the Phase 2 INDIGO clinical trial of maralixibat in PFIC. An analysis of response as determined by a 75% reduction in sBA showed that maralixibat responders had a significant improvement in transplant free survival. In addition, maralixibat responders exhibited significant improvements in pruritus and growth. Our MAA also included a five-year analysis of PFIC2 patients treated with maralixibat compared to a natural history control cohort showing an improvement in event free survival with maralixibat. Maralixibat has been granted orphan drug designation for PFIC by the FDA and the EMA. In addition, we are conducting the MARCH-PFIC Phase 3 clinical trial of maralixibat in PFIC. The MARCH-PFIC clinical trial and long-term extension MARCH-ON is evaluating maralixibat at higher doses in multiple PFIC subtypes. We expect to complete enrollment in MARCH-PFIC in the second quarter of 2021 and report topline data in early 2022.

Maralixibat in BA

BA is a rare liver disorder in which there is a blockage or absence of large bile ducts that leads to bile accumulation in the liver and results in progressive cholestasis and liver damage. BA occurs in infants and is estimated to affect one in every 10,000 to 15,000 live births in the United States. BA is the most common reason for liver transplantation in children. There remains a substantial unmet medical need for therapeutic interventions as initial surgical treatment is often unsuccessful. The standard of care for BA is the Kasai procedure, a surgery in which a segment of the small intestine is used to attach the small intestine directly to the liver where bile is expected to drain and is most successful if conducted in the first eight weeks of life. The success rate for the Kasai procedure is approximately 30% to 40%, while the remaining patients are at risk of progressive liver disease requiring liver transplantation. Prognosis after Kasai procedure has been shown to be most promising in patients with lower levels of bilirubin. Further, a strong association between sBA control post-Kasai procedure with long-term outcomes has been observed, supporting the hypothesis that pharmacologically reducing sBA may improve outcomes in BA. We believe ASBT inhibition has therapeutic potential in this patient population through its impact on sBA. We initiated recruitment for the EMBARK Phase 2b clinical trial of maralixibat in BA in the first quarter of 2021. Maralixibat has been granted orphan drug designation for BA by the FDA and the EMA.

Volixibat

We are advancing our second product candidate, volixibat, a novel, oral, minimally-absorbed agent designed to inhibit ASBT, for the treatment of adult patients with cholestatic liver diseases. We are developing volixibat for the treatment of ICP, PSC and PBC. Volixibat has been studied in over 400 adults for up to 48 weeks. Clinical trials of volixibat have shown significant activity on ASBT and bile acid markers such as 7 α C4, fecal bile acids and cholesterol, demonstrating potent biological activity.

ICP is diagnosed in pregnant women typically during the second or third trimester and increases the risk of stillbirth, preterm labor and neonatal complications. Additionally, ICP is associated with severe pruritus. In ICP, sBA levels have been shown to correlate with worsened risk of pre-term labor and stillbirth. We estimate that each

year there are approximately 40,000 cases of ICP in the United States and approximately 100,000 cases of ICP in Europe. We have initiated recruitment for the OHANA clinical trial of volixibat in ICP. OHANA is an adaptive, randomized Phase 2b clinical trial evaluating the effect of volixibat on sBA, pruritus and perinatal outcomes in patients with ICP.

PSC is a serious, idiopathic chronic cholestatic liver disease characterized by the progressive inflammation and destruction of bile ducts, which can lead to life-threatening complications. It is estimated that approximately 29,000 people in the United States and approximately 50,000 people in Europe suffer from PSC. Up to 70% of PSC patients suffer from pruritus during the course of the disease. Liver transplantation is the only treatment shown to improve clinical outcomes in PSC but is expensive, requires long-term administration of immuno-suppressants and only a portion of the patients who require a liver transplant are able to match with a suitable donor organ. Ursodeoxycholic acid (“UDCA”), is used off-label in PSC with conflicting evidence. We dosed the first patient in the VISTAS Phase 2b clinical trial of volixibat in PSC in January 2021. VISTAS is an adaptive, randomized Phase 2b clinical trial evaluating the effect of volixibat on pruritus, sBA and fibrosis markers in patients with PSC and pruritus.

PBC is a chronic, rare, cholestatic liver disease characterized by progressive liver bile flow impairment caused by immune-mediated destruction of intrahepatic bile ducts. This results in increased hepatic bile acid concentrations, which leads to a local inflammatory response in the liver that progresses to hepatic fibrosis, cirrhosis, and hepatic decompensation. The incidence rates for PBC in Europe, North America, Asia, and Australia are reported as ranging from 0.33 to 5.8 per 100,000 people, with a prevalence ranging from 1.91 to 40.2 per 100,000 people. We plan to initiate the Phase 2b clinical trial of volixibat in PBC in the second half of 2021.

There are no approved therapies for PSC or ICP in the United States. A variety of licensed and off-label therapies are currently used to reduce the impact of the progressive nature of PBC. These include UDCA, obeticholic acid, peroxisome proliferator activator receptors like bezafibrate and fenofibrate, and others. However, the few therapeutic options available to manage PBC associated pruritus are temporary and/or suboptimal.

Our History

Our mission is to develop life-changing therapies for patients suffering from debilitating liver diseases. Our management team has significant experience in progressing liver and orphan diseases therapies from early stage research to clinical trials and ultimately to regulatory approval and commercialization. In May 2018 we were incorporated in Delaware and began operations in November 2018. In July 2019, we completed our initial public offering (“IPO”). Our team has extensive experience developing and commercializing medicines, including in hepatology settings.

Our Strategy

Our goal is to be a leader in the treatment of liver diseases for which the unmet medical need is high. The key components of our strategy include:

- **Advance maralixibat through clinical development and seek regulatory approvals for the treatment of ALGS, PFIC and BA.** Results from our Phase 2b ICONIC trial demonstrated maralixibat’s potential to provide benefits in patients with ALGS. Based on these data, we completed a submission of an NDA for the treatment of cholestatic pruritus in patients with ALGS in January 2021 and if accepted we anticipate approval and subsequent launch in the second half of 2021. We have also submitted an MAA for maralixibat for PFIC2 in Europe and, if approved, plan to commercialize maralixibat in Europe in early 2022. We are also conducting the MARCH-PFIC Phase 3 clinical trial to evaluate maralixibat at a higher dose and in additional PFIC subtypes. We are also evaluating the potential of maralixibat in the EMBARK Phase 2b clinical trial in BA.
- **Advance volixibat for the treatment of adults with PSC, ICP and PBC.** We plan to further leverage our understanding of cholestatic liver disease with volixibat in adult settings. We initiated clinical trials in ICP and PSC in the first quarter of 2021 and plan to initiate a clinical trial in PBC in the second half of 2021.

- **Commercialize our product candidates, if approved, in North America and Europe.** We have retained all worldwide commercial rights for maralixibat and volixibat. Given the targeted prescribing nature of the indications we are currently pursuing, we believe we will be able to independently commercialize maralixibat and volixibat in North America and Europe with a targeted specialty sales force. We plan to seek strategic collaborations or partnerships with larger biopharmaceutical companies or those specialized in the relevant areas for territories outside North America and Europe.
- **Actively manage our product portfolio and expand our pipeline of novel product candidates.** We believe the mechanism of action of maralixibat and volixibat has utility for the treatment of additional cholestatic liver diseases. We have assembled an executive team of scientific, clinical and business leaders with highly relevant experience to enable the advancement of therapeutics in the field of liver diseases. We intend to leverage our collective expertise to identify, acquire, in-license and advance additional product candidates for the treatment of liver diseases.

Overview of Cholestatic Liver Diseases

The liver is responsible for many vital body functions, including the regulation of bile acid synthesis and metabolism. The liver uses cholesterol to produce bile acids, which promote digestion and absorption of dietary fats and fat-soluble vitamins. Approximately 95% of bile acids recirculate back to the liver, and the remaining bile acids are excreted from the body in the feces. ASBT is present in the small intestine and mediates the uptake of bile acids in the intestines and recycles them back to the liver.

In patients with cholestatic liver diseases, the flow of bile from the liver is impaired. Accumulation of bile acids in the liver leads to liver injury, progressive liver disease and, if left untreated, results in fibrosis, cirrhosis, liver failure and death. Patients often experience debilitating pruritus, which dramatically impacts quality of life and can lead to epidermal scarring, sleep deprivation, significant fatigue and psycho-social effects. In some patients, intractable pruritus can be severe enough to be an indication for liver transplantation. Caregivers, particularly parents of children with cholestatic liver diseases, also suffer from impaired sleep and anxiety as they struggle to help their loved ones manage these debilitating symptoms. Other general manifestations of cholestatic liver diseases include jaundice, progressive liver disease and growth delay.

Alagille Syndrome

ALGS is a rare genetic disorder in which bile ducts are abnormally narrow, malformed and reduced in number, which leads to bile accumulation in the liver and ultimately progressive liver disease. The estimated incidence of ALGS is one in every 30,000 births in the United States and Europe. Based on primary research conducted with pediatric hepatologists and gastroenterologists, the specialist physicians who typically treat ALGS, we believe the initial addressable patient population in the United States will be a subset of these patients, comprising approximately 2,000-2,500 pediatric ALGS patients. We believe this addressable number may grow with the availability of an oral therapy as an alternative to transplant for the treatment of pruritus due to ALGS as well as increased disease awareness and diagnosis.

In patients with ALGS, multiple organ systems may be affected by the mutation, including the liver, heart, kidneys and central nervous system. The accumulation of bile acids prevents the liver from working properly to eliminate waste from the bloodstream and leads to progressive liver disease. Signs and symptoms arising from cholestasis in ALGS may include jaundice, pruritus, xanthomas and growth deficit. The pruritus experienced by patients with ALGS is among the most severe in any chronic liver disease and is present in most affected children by the third year of life. In children with cholestasis due to ALGS, it is estimated that only about 25% will survive past 18 years of age with their native liver. Furthermore, it is reported that the majority of liver transplants in ALGS are due to cholestatic symptoms rather than progressive liver damage. In patients who have not received a liver transplant, 75% have active scratching, with 32% having destruction of skin, bleeding or scarring. Children with ALGS experience a markedly impaired quality of life largely due to the intense pruritus and associated skin lesions and disruptions in sleep and mood. A study to assess the health-related quality of life in ALGS patients indicated a significant burden in physical, psychological and social health accompanies the disease.

There remains a substantial unmet medical need for therapeutic options for ALGS, as PEBD and liver transplantation are the only options available for these patients.

Progressive Familial Intrahepatic Cholestasis

PFIC is a rare genetic disorder that causes cholestasis and progressive liver disease, which typically leads to liver failure. The disease is inherited in an autosomal recessive pattern, meaning mutations in both copies of the gene are necessary to cause the disorder. PFIC is estimated to affect one in every 50,000 to 100,000 births in the United States and Europe. Based on primary research conducted with pediatric hepatologists and gastroenterologists, the specialist physicians who typically treat PFIC, we believe the initial addressable patient population in the United States is approximately 500-750 PFIC2 children.

In patients with PFIC, liver cells have a diminished ability to secrete bile due to mutations in proteins that control bile flow. The resulting buildup of bile in liver cells causes liver damage in affected individuals. Six types of PFIC have been genetically identified, all of which are similarly characterized by impaired bile flow and progressive liver disease. Our initial focus is on the nt-PFIC2, or bile salt export pump (“BSEP”) protein deficient, patient population, which accounts for approximately 50% of the PFIC patient population. PFIC2 is caused by a mutation in the ABCB11 gene, which normally encodes a BSEP protein that transports bile acids out of the liver. Mutations in the ABCB11 gene result in the buildup of bile salts in liver cells, damaging these cells and causing liver disease. Patients with nt-PFIC2 have mutations in ABCB11 that are expected to have some residual BSEP function and thus an ability, though impaired, to transport some bile acids to canaliculus, gall bladder and small intestines where maralixibat is active.

Signs and symptoms of PFIC typically begin in infancy and are related to buildup of toxic bile acid in the liver. Patients with PFIC experience pruritus, jaundice, failure to gain weight and to grow at the expected rate, enlarged livers and spleens and progressive liver disease. Elevation of sBA is a common feature of the disease. Children with PFIC2 often develop liver failure within the first few years of life and have an increased risk of developing liver cancer. The most prominent and troublesome ongoing symptom of PFIC is severe pruritus, leading to a greatly diminished quality of life.

There remains a substantial unmet medical need for therapeutic options for PFIC, as PEBD and liver transplantation are often the sole options available for patients. Children with nt-PFIC2 are our initial target patient population for treatment with maralixibat. We believe the opportunity exists to broaden beyond this initial patient population, and we are evaluating the effectiveness of maralixibat in patients with other types of PFIC, such as PFIC1 and PFIC3, in a supplemental cohort in our Phase 3 MARCH trial.

Benign recurrent intrahepatic cholestasis (“BRIC”), consists of two types, BRIC1 and BRIC2, which have the same underlying genetic mutations as PFIC1 and PFIC2, respectively. BRIC is characterized by intermittent episodes of cholestasis with pruritus. This condition is called benign because it typically does not cause lasting damage to the liver, but it can develop into a more severe, permanent form. There are no approved therapies for BRIC, but patients can achieve temporary relief of the severe pruritus by lowering bile acid levels through procedures such as naso-biliary drainage. We believe there is therapeutic potential for an ASBT inhibitor (“ASBTi”), for the treatment of pruritus associated with BRIC.

Biliary Atresia

BA is a rare liver disorder in which there is a blockage or absence of large bile ducts that leads to bile accumulation in the liver and ultimately results in progressive cholestasis and liver damage. BA occurs in infants and is estimated to affect one in every 10,000 to 15,000 live births in the United States. BA is the most common reason for liver transplantation in children.

The underlying causes of BA are not completely understood. For some patients, BA may occur because the bile ducts did not form properly during fetal development and in others, inflammation around the time of birth leads to destruction of bile ducts. As a result of BA, bile acids are not able to adequately drain from the liver, resulting in an array of signs and symptoms shortly after birth, including jaundice, dark urine and enlarged liver. The rapid progression of BA necessitates surgical intervention within the first months of life.

There remains a substantial unmet medical need for therapeutic interventions, as invasive surgery is often unsuccessful. The standard of care for BA is the Kasai procedure, a surgery in which a segment of the small intestine is used to attach the small intestine directly to the liver where bile is expected to drain and is most successful if conducted in the first eight weeks of life. The success rate of the Kasai procedure is approximately 30% to 40%. The remaining patients are at risk of progressive liver disease requiring liver transplantation, often before two years of age. Recent analyses of outcomes in post-Kasai procedure BA have shown that the risk of progression to transplant is higher in patients with elevated sBAs or bilirubin.

Intrahepatic Cholestasis of Pregnancy

ICP is a liver disorder that occurs in pregnant women, often during the third trimester, which impairs the normal release of bile from liver cells and leads to impaired liver function. We estimate that each year there are approximately 40,000 cases of ICP in the United States and approximately 100,000 cases of ICP in Europe. ICP can contribute to serious complications, including preterm labor, stillbirth and neonatal complications.

The underlying cause of ICP is not completely understood, but it is thought that the increase in pregnancy hormones during the second and third trimesters impairs liver function and the flow of bile. Also, some women have a genetic profile similar to that seen in PFIC. The disease can result in intense pruritus, typically of the hands and feet. It resolves rapidly following birth but can cause serious complications for childbirth, including meconium-stained amniotic fluid, preterm labor, neo-natal asphyxia and stillbirth. The rates of these events increase with increasing levels of maternal sBA. Induction of early delivery, i.e. before 36 gestational weeks, is an option for high risk pregnancies but bear the risk of long-term consequences for the child.

Due to the acute nature of the disease and potential for complications during pregnancy, there remains an unmet medical need for a safe and effective treatment option for ICP. There is no approved therapy for ICP in the United States, but UDCA is used off-label to decrease the concentration of harmful bile acids. However, reports suggest that UDCA offers minimal improvement for patients. Therefore, patients with ICP may benefit from treatment with an ASBTi.

Primary Sclerosing Cholangitis

PSC is a rare, serious, idiopathic chronic cholestatic liver disease characterized by progressive inflammation and destruction of bile ducts, which may lead to fibrosis, cirrhosis, portal hypertension, cancer and ultimately liver failure. It is estimated that approximately 29,000 people in the United States and approximately 50,000 people in Europe suffer from PSC.

The underlying cause of PSC is not completely understood, but it is thought to arise from a combination of genetic and environmental factors. There is evidence that variations in certain genes involved in immune function increase the risk of developing PSC. The median age at diagnosis is approximately 35 years and approximately 70% of PSC patients have inflammatory bowel disease, principally ulcerative colitis.

The earliest symptoms of PSC include extreme fatigue, abdominal discomfort and pruritus. Up to 70% of PSC patients suffer from pruritus during the course of the disease. As the condition worsens, patients may develop jaundice and enlarged spleens. Eventually, the buildup of bile damages liver cells and contributes to progression of the disease from chronic liver disease to subsequent liver failure. Median transplant-free survival for PSC patients is estimated to be nine to 18 years from diagnosis in symptomatic patients, depending upon the stage of the disease at the time of diagnosis. Complications involving the biliary tree are common and include cholangitis, as well as ductal strictures and gallstones, both of which may require frequent endoscopic or surgical interventions. PSC increases the risk of development of malignancies, with cholangiocarcinoma, a group of cancers that begin in the bile ducts, being the most common.

There is an acute need for novel therapeutic interventions in PSC as liver transplantation is currently the only known treatment shown to improve clinical outcomes. UDCA is often used off-label for the treatment of PSC but does not offer improvement in pruritus, one of the most debilitating symptoms associated with the disease. PSC is the fifth leading indication for liver transplantation; however, the post-transplant recurrence rate of PSC is as high as

25%. We believe an ASBTi offers a substantial opportunity to address many of the symptoms and associated complications of PSC, as well as potentially delay or eliminate the need for liver transplantation.

Primary Biliary Cholangitis

PBC is a chronic, rare, cholestatic liver disease characterized by progressive liver bile flow impairment caused by immune-mediated destruction of intrahepatic bile ducts. This results in increased hepatic bile acid concentrations, which leads to a local inflammatory response in the liver that progresses to hepatic fibrosis, cirrhosis, and hepatic decompensation. Patients with PBC progress at varying rates, some becoming decompensated over a period of several years while others progress over more than a decade. If left untreated or not optimally treated, chronic cholestasis and bile-duct destruction from PBC can cause liver failure and result in ultimately liver transplantation or death. The pathogenesis of PBC is unknown, though the breakdown of immune self-tolerance is proposed as the disease is characterized by a T-lymphocyte mediated attack on intralobular bile ducts. It is believed that genetic susceptibility and environmental factors may cause PBC.

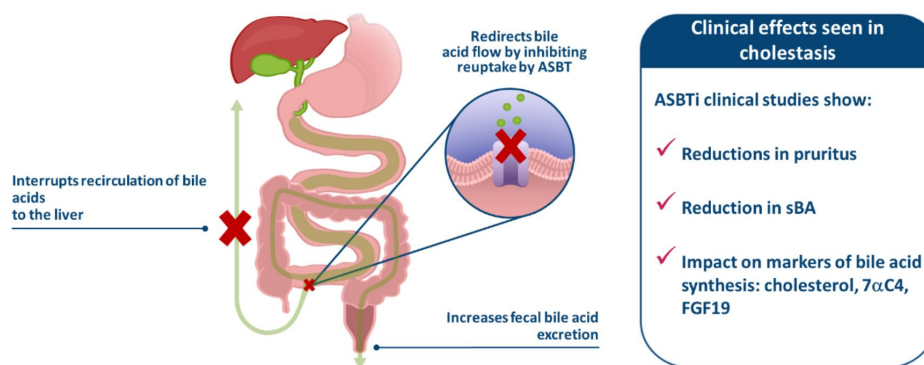
PBC disproportionately affects women at a ratio of 10:1. The incidence rates for PBC in Europe, North America, Asia, and Australia are reported as ranging from 0.33 to 5.8 per 100,000 inhabitants, with a prevalence ranging from 1.91 to 40.2 per 100,000 inhabitants. PBC is typically diagnosed in patients between 40 to 60 years of age, with those who are younger at onset or male having a worse prognosis. The estimated average time from first appearance of the hallmark serologic signature, antimitochondrial antibodies (“AMA”), to death is approximately 20 years to 22 years without treatment.

Patients with pruritic PBC often experience a significant reduction in quality of life and impairment of sleep. Severe pruritus limits daily activities, causes fatigue, depression, and, in some cases, suicidal ideation. Studies report that up to 70% of patients with PBC experience pruritus and about 75% of patients experience pruritus before diagnosis.

A variety of licensed and off-label therapies are currently used to reduce the impact of the progressive nature of PBC. These include UDCA, obeticholic acid, peroxisome proliferator activator receptors like bezafibrate and fenofibrate, and others. However, the few therapeutic options available to manage PBC associated pruritus are temporary and/or suboptimal. First-line (bile-acid sequestrants) and second-line (rifampicin, opiates, SSRIs) therapies have demonstrated partial efficacy but are associated with tolerability issues, side-effect concerns or have drug-drug interactions. Lastly, antihistamines are widely used but provide only temporary pruritic relief. In severe cases of pruritus refractory to medical treatments, biliary drainage can be used to alleviate pruritus and can be an indication for liver transplantation as a last resort.

Our Solutions

Cholestatic liver diseases are driven by increased levels of bile acids. As depicted in the figure below, inhibiting ASBT results in more bile acids being excreted in the feces, leading to lower levels of bile acids systemically and thereby reducing bile acid mediated liver damage. This leads to improvements in liver function, pruritus and other symptoms of cholestatic liver diseases.



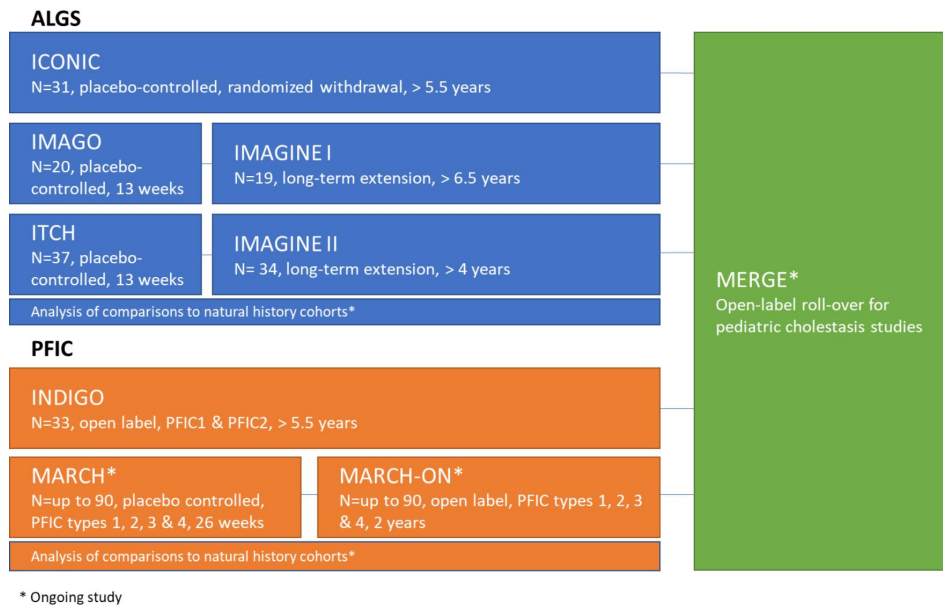
Overview of Maralixibat

Our lead product candidate, maralixibat, is a novel, oral, minimally-absorbed agent designed to selectively inhibit ASBT. Maralixibat possesses an extensive safety dataset, having been evaluated in more than 1,600 human subjects.

Maralixibat has been studied in 86 pediatric patients with ALGS across five Phase 2 clinical trials, including three placebo-controlled clinical trials. The first two ALGS clinical trials of maralixibat, at low doses, showed signs of activity; however, their primary endpoints were not met, although long term analysis showed sustained control of pruritus and sBA. In the Phase 2b ICONIC clinical trial of maralixibat in ALGS, patients taking maralixibat had statistically significant reductions in pruritus and sBA compared to placebo. At the 48-week measurement, pruritus and sBA reductions were maintained and improvements in xanthomas and quality of life were also observed. We are pursuing full approval from the FDA for the indication of cholestatic pruritus in patients with ALGS.

In addition to the ongoing Phase 3 MARCH clinical trial, maralixibat has been studied in 33 pediatric patients with PFIC in one open-label Phase 2 clinical trial. Results from the Phase 2 INDIGO clinical trial of maralixibat in PFIC showed multi-parameter response in patients with nt-PFIC2 on pruritus, sBA, normalization of liver enzymes if abnormal at baseline and quality of life scores, which was the basis for maralixibat's breakthrough therapy designation for the treatment of PFIC2. While the primary endpoint of sBA change from baseline to week 13 did not reach statistical significance for the overall group, the pre-specified 48-week analysis of the clinical trial demonstrated a profound treatment response in a subset of PFIC2 patients. A long-term analysis of the INDIGO clinical trial showed control of sBA with maralixibat in patients with PFIC2 led to transplant free survival in line with literature stating that sBA control with surgical biliary diversion has demonstrated 15-year transplant free survival. In addition, an improvement in growth compared to a normalized growth curve for those patients who had a response in sBA and pruritus. In a natural history comparison between INDIGO and a PFIC2 natural history cohort showed improved event free survival with maralixibat. We commenced enrollment in the Phase 3 MARCH clinical trial of maralixibat in PFIC in the second quarter of 2019, with a primary endpoint focused on pruritus in patients with nt-PFIC2.

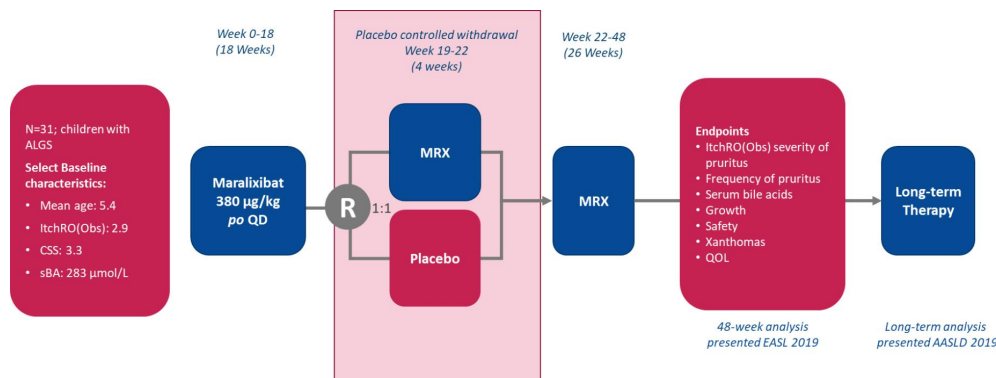
Maralixibat has been studied in a number of pediatric clinical trials.



Our Clinical Trials of Maralixibat in ALGS

Phase 2b ICONIC Trial

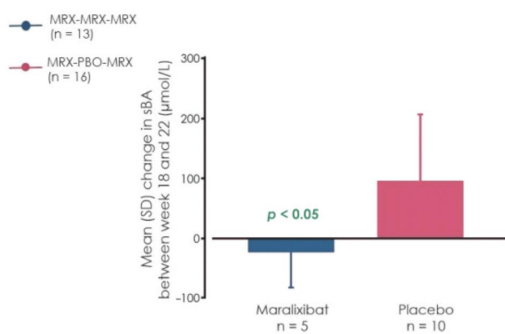
The multicenter Phase 2b ICONIC clinical trial has a four-week double-blind, randomized, placebo-controlled drug withdrawal period with the following design:



The ICONIC clinical trial enrolled 31 ALGS patients with sBA greater than three times the upper limit of normal and moderate to severe pruritus and includes an open-label extension period of over four years. The ICONIC clinical trial met its primary endpoint of a mean change in sBA between placebo and maralixibat during the

randomized drug withdrawal period in responders, as defined in the graph below. A statistically significant difference in sBA was observed between the treatment groups ($p < 0.05$).

Change in sBA during the randomized drug withdrawal period in sBA responders (responders defined as 50% reduction in sBA at week 12 or 18)

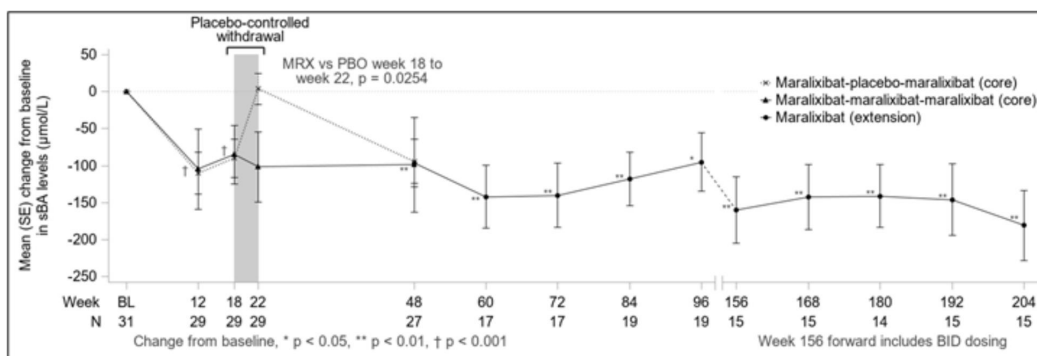


MRX=maralixibat; PBO=placebo

The ICONIC trial demonstrated statistical significance on efficacy measures at multiple timepoints. In addition to the primary endpoint, the ICONIC clinical trial evaluated measures of pruritus, sBA and xanthomas.

In the ICONIC trial, sBA changes were evaluated in the full study population over time as a measure of the bile acid reduction activity of maralixibat. As depicted in the figure below, at week 18, patients treated with maralixibat experienced an approximately 31% mean reduction from baseline in sBA levels in the overall study population. During the randomized withdrawal period, patients treated with placebo experienced a significant increase in sBA levels to near baseline levels, whereas patients who continued on maralixibat maintained their reduction in sBA levels at week 22 ($p < 0.05$). After the randomized drug withdrawal phase, placebo patients received maralixibat for a second time. At week 48, placebo patients experienced a 36% mean sBA reduction compared to sBA levels at week 22. Reductions in sBA were sustained through week 204.

Mean reductions from baseline in sBA levels

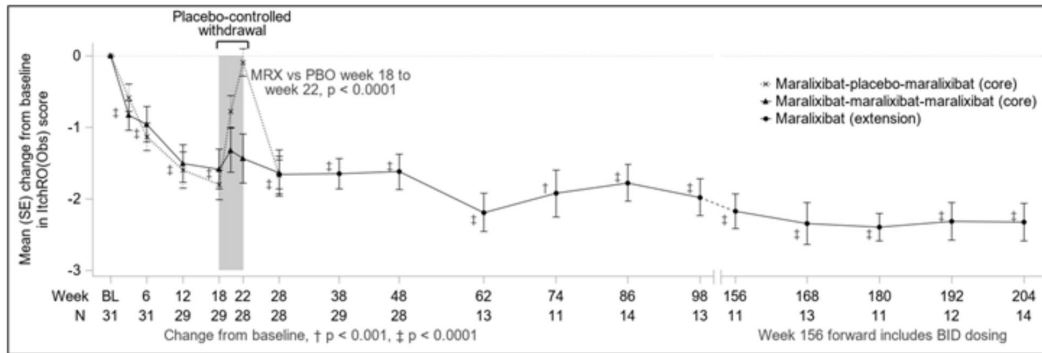


As depicted in the figure below, patients treated with maralixibat experienced an approximately 60% mean reduction from baseline to week 18 in pruritus, as measured by ItchRO(Obs) score ($p < 0.0001$). The predefined analysis to assess changes in pruritus during the randomized drug withdrawal period showed that patients who were randomized to placebo experienced a recurrence of their pruritus, whereas those who continued on maralixibat

maintained their reduction in pruritus ($p < 0.0001$). After the randomized drug withdrawal phase during which placebo patients received maralixibat for a second time, a decrease in ItchRO(Obs) score similar to those who had received continuous maralixibat treatment was observed. The results during the randomized drug withdrawal period demonstrate a treatment effect with maralixibat. Pruritus improvements were maintained through week 48 and were statistically significant as compared to baseline ($p < 0.0001$) and were sustained through week 204.

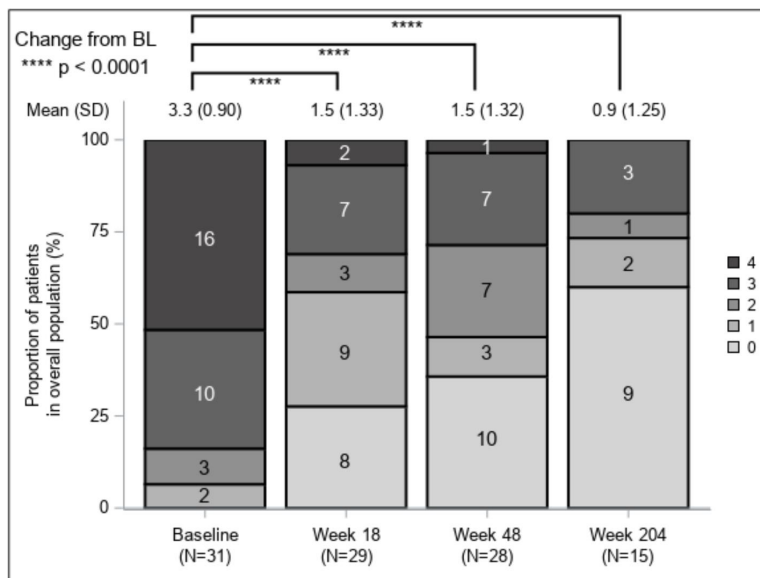
The ItchRO(Obs) score is a caregiver-reported outcome assessment developed for use in cholestatic liver diseases, which measures severity of itch on a 0-4 scale. The ItchRO(Obs) score is a tool developed for evaluating pruritus in pediatric cholestatic settings. Over the course of the maralixibat program, ItchRO(Obs) has been developed and tested to support an outcome assessment for regulatory purposes. We have incorporated FDA input into the use of the tool in our clinical trials. Our validation work with ItchRO(Obs) supports that a change of 1.0 is clinically meaningful.

Observer-reported pruritus severity ItchRO(Obs) weekly average morning score change from baseline



The ICONIC trial analysis evaluated additional measures of pruritus to further characterize the potential treatment effects of maralixibat. The clinician scratch score (“CSS”), is a measure of itch evaluated by the treating physician. The CSS uses a scale of 0-4 in which 0=none, 1=rubbing or scratching, 2=active scratching without evident skin abrasions, 3=abrasions evident and 4=cutaneous mutilation, hemorrhage and scarring. Results were consistent with the pruritus ItchRO(Obs) results during both the blinded drug withdrawal period and at the end of the 48-week observation period. The proportion of patients with the maximum CSS score of 4 decreased from 51.6% at baseline to 6.9% at week 18 and remained stable at 7.1% at week 48. Statistically significant mean reductions from baseline were noted in the overall study population from baseline to week 204, indicating durable improvement in pruritus. The results are shown below and provide further evidence of a treatment effect with maralixibat.

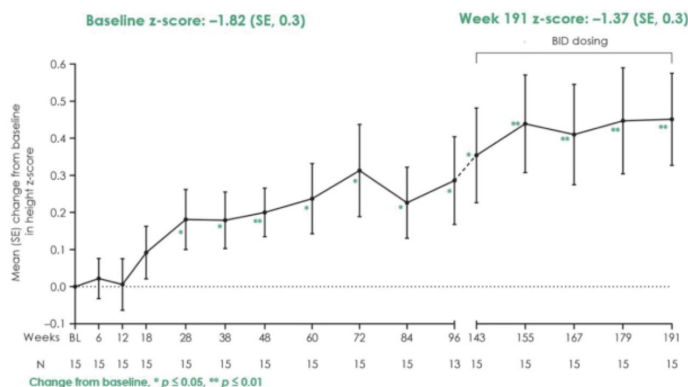
Improvements from baseline in Clinician Scratch Scale scores



The ICONIC trial also evaluated xanthomas on the Clinician Xanthoma Scale, which uses a 5-point scale that ranges from 0 (none) to 4 (disabling). Xanthomas are cholesterol deposits underneath the skin that occur as a result of retained bile acids and cholesterol in some ALGS patients and can be very disfiguring and debilitating. In the ICONIC clinical trial, maralixibat led to a mean reduction of 44% in xanthoma score at week 48 as compared to baseline ($p < 0.01$). Additionally, of the patients who had xanthomas at baseline, 43% had no xanthomas at week 48.

In addition, xanthomas ($p < 0.05$) remained significantly reduced compared to baseline with long-term treatment. Improvements were also seen in the PedsQL Multidimensional Fatigue Scale score ($p < 0.01$). As depicted in the figure below, children taking maralixibat exhibited a clinically meaningful and statistically significant acceleration in height growth as measured by height z-score ($p \leq 0.01$). In ICONIC, the mean height percentile for patients followed to week 191 increased from the 9th percentile to the 16th percentile. Maralixibat was generally well tolerated at doses of up to 760 $\mu\text{g}/\text{kg}/\text{day}$.

Increased height z-scores with long-term maralixibat treatment



Additional Phase 2 Trials in ALGS

Two additional clinical trials have been conducted for maralixibat for the treatment of ALGS. These clinical trials included dose-ranging randomized assessments of maralixibat compared to placebo at week 13 on measures of sBA and pruritus. All of the dose levels of maralixibat evaluated in the randomized comparison were lower than those used in the ICONIC clinical trial. We believe the dose of 380 µg/kg used in the ICONIC clinical trial has the potential for stronger therapeutic activity on pruritus than the lower doses evaluated in these clinical trials. The table below summarizes the pruritus results from the Phase 2 ITCH and IMAGO clinical trials of maralixibat in ALGS.

	ITCH MRX Week 13	ITCH PBO Week 13	IMAGO MRX Week 13	IMAGO PBO Week 13
MRX (µg/kg QD)	133/266	0	133/266	0
Change from Baseline ItchRO(Obs)	-1.19	-0.58	-0.61	-0.59
% Change from Baseline ItchRO(Obs)	-39%	-21%	-22%	-19%

Long-term analysis from IMAGINE I, the extension of the IMAGO clinical trial, showed that despite there not being a significant difference from placebo at week 13, pruritus relief was sustained over the long-term open label treatment with maralixibat. Similarly, in the long-term extension of ITCH, IMAGINE II, reductions in ItchRO(Obs) and CSS were observed at week 48 and sustained for up to 216 weeks.

Registrational Path for Maralixibat in ALGS

We completed our submission of an NDA for the treatment of cholestatic pruritus in patients with ALGS in January 2021. We have received breakthrough therapy designation for maralixibat for the treatment of pruritus associated with ALGS in patients one year of age and older. In November 2019, we were granted Rare Pediatric Disease Designation for maralixibat for ALGS, and as a result, we may qualify for the receipt of a priority review voucher if our NDA is approved.

In addition, we plan to further discuss our submission plans with the EMA after further analysis of our long-term extension treatment data compared to natural history data.

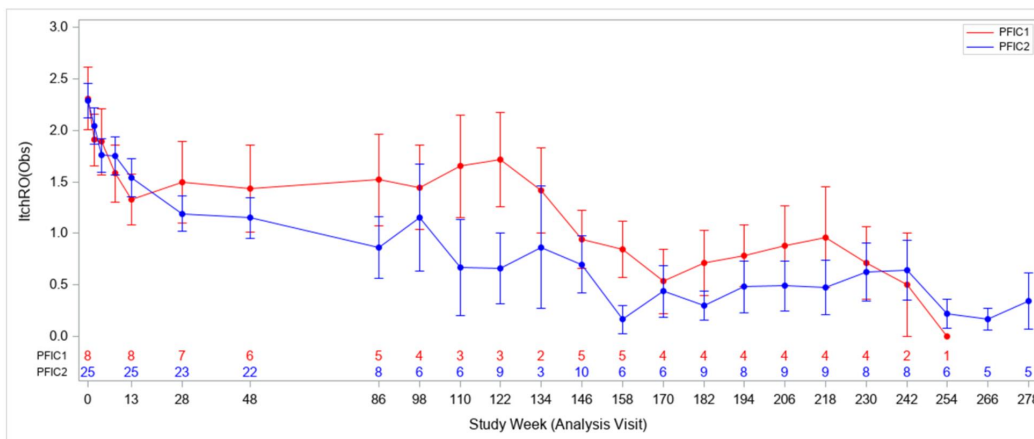
Our Clinical Trials of Maralixibat in PFIC

Phase 2 INDIGO Trial

The Phase 2 INDIGO clinical trial is a long-term, open-label trial designed to evaluate the safety and efficacy of maralixibat in 25 pediatric patients with PFIC2 and eight pediatric patients with PFIC1. Treatment response on sBA, pruritus and growth paired with 5-year transplant free and event free survival improvements from INDIGO served as the basis of our MAA submission to EMA for maralixibat for PFIC2. INDIGO evaluated measures of sBA and pruritus at various time points. The primary endpoint of the change from baseline to week 13 in fasting sBA level did not reach statistical significance for the overall group, but profound and durable reductions in sBA were seen in patients with PFIC2 at 48 weeks and maintained long term. The secondary endpoint of a reduction from baseline to week 13 in pruritus as measured by the ItchRO(Obs) scale did reach statistical significance for the overall group. Moreover, in the 48-week analysis, 55% of PFIC2 patients had a clinically meaningful pruritus reduction as measured by the ItchRO(Obs) scale. Patients are currently being followed in a long-term extension trial. During the INDIGO clinical trial, maralixibat was administered at doses up to 266 µg/kg daily ("QD"). Patients without response or with partial treatment response could escalate to 266 µg/kg twice daily ("BID").

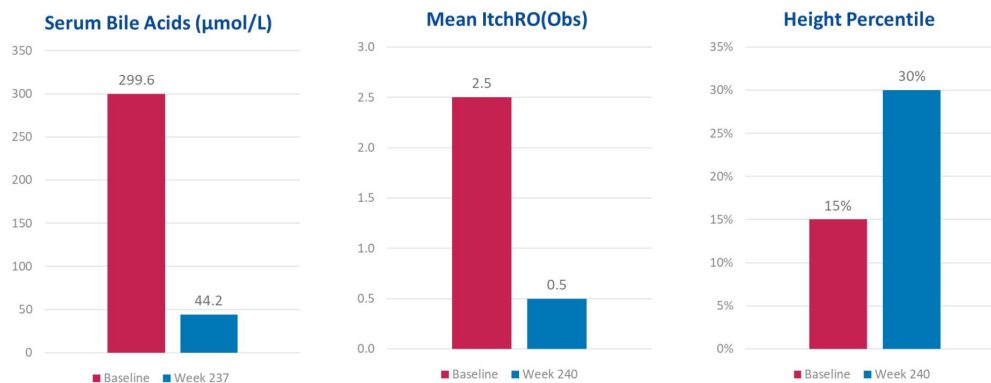
The chart below show the ItchRO(Obs) response profiles for the patients with PFIC1 and PFIC2.

ItchRO(Obs) Reported Pruritus Scores Over Time – PFIC 1 and 2



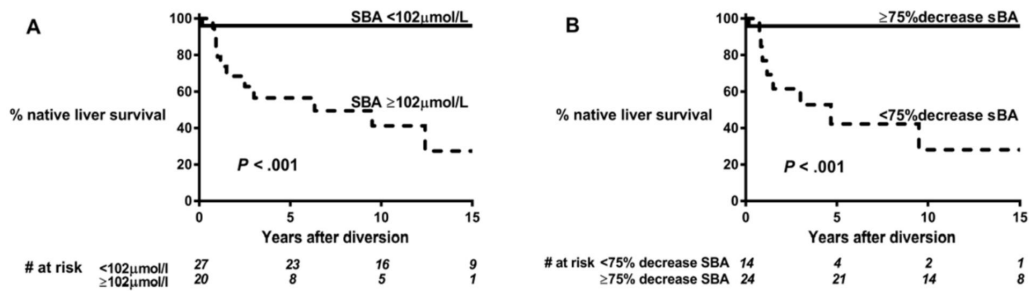
The responses observed in the PFIC2 patient group provided the basis for breakthrough therapy designation for the treatment of PFIC2 patients. At the 48-week time point, maralixibat treatment in PFIC2 responders led to normalization (<8.5 $\mu\text{mol/L}$) or significant reduction (>70%) in sBA levels from baseline and control of pruritus (1.0 point reduction from baseline on the ItchRO(Obs) scale). This pattern of improvement has not been observed in the natural history of the disease. An analysis of PFIC2 patients with complete absence of BSEP function, that is, patients with a truncating mutation in the PFIC2 gene (“truncating PFIC2”), showed that these patients were unlikely to respond to treatment, whereas those patients with residual BSEP function, that is, patients with nt-PFIC2 had the greatest reductions in both sBA and pruritus. Of the 19 nt-PFIC2 patients in the clinical trial, seven had a durable sBA response, with a mean reduction to 44.2 $\mu\text{mol/L}$ (from a baseline of 299.6 $\mu\text{mol/L}$). A corresponding reduction in ItchRO was observed along with durable improvements in growth as outlined in the graphics below.

sBA response is associated with multi-parameter improvements

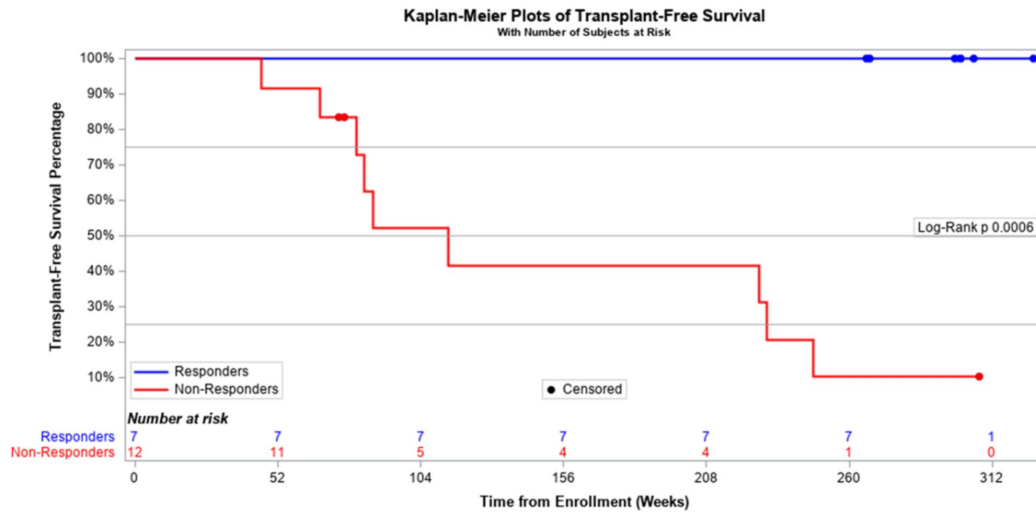


sBA response has also been shown to predict transplant-free survival in a retrospective natural history analysis. The analysis included 264 PFIC2 pediatric patients with homozygous or compound heterozygous pathogenic ABCB11 mutations. sBAs were established as a predictive marker of long-term transplant-free survival after interruption of enterohepatic circulation. This clinical trial demonstrates nt-PFIC2 patients who had a significant reduction and control of sBAs (defined as sBA threshold of less than 102 $\mu\text{mol/L}$ or a 75% reduction) after

interruption of the enterohepatic circulation via PEBD remained transplant-free out to 15 years post-SBD. Patients in whom SBD did not lead to such control of sBA levels had significantly worse native liver survival with approximately 50% and 70% of the group under-going liver transplant or death within five and 15 years, respectively.



Akin to these effects observed in NAPPED, the same sBA response profile was observed after pharmacological interruption of the enterohepatic circulation with maralixibat treatment responders (see figure below). The data from a five year analysis of INDIGO below indicate that 100% of maralixibat patients who achieved the established NAPPED sBA response threshold remained transplant free, whereas those who did not achieve the sBA response criteria went on to eventually receive a liver transplant. The difference between the groups was statistically significant (p=0.0006). We believe that the INDIGO data show a clear pattern of response in patients with PFIC2 leading to long-term transplant free survival. In addition to the INDIGO data, through an academic collaboration, a comparison of event free survival of maralixibat to a natural history cohort of patients was conducted showing an advantage in event free survival for the maralixibat group.

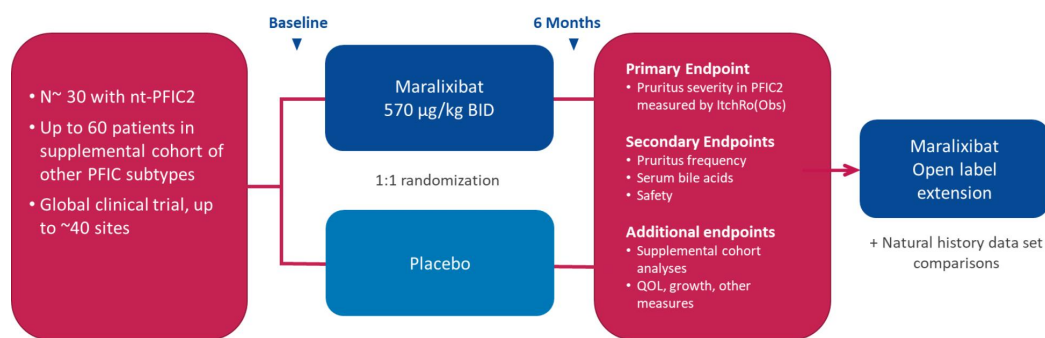


Registrational Program for Maralixibat in PFIC

We have submitted the results of the INDIGO clinical trial and natural history comparisons as part of an MAA to the EMA for maralixibat for the treatment of PFIC2. The MAA submission has been validated as of November 2020 and is under review as of the date of this Annual Report.

We are also conducting the Phase 3 MARCH clinical trial to evaluate higher doses of maralixibat and additional PFIC sub-types. MARCH is a randomized, placebo-controlled clinical trial of maralixibat in PFIC. As

depicted in the figure below, the clinical trial is evaluating maralixibat at a dose of up to 570 µg/kg BID compared to placebo for six months followed by a long-term open label extension in which all patients will receive maralixibat. The primary endpoint is a reduction in severity of pruritus as measured by the ItchRO(Obs) scale and will include up to 30 patients with nt-PFIC2 aged one to 17 years. Other PFIC patients who do not meet the inclusion criteria for the primary cohort but otherwise meet eligibility criteria will be enrolled in a supplemental cohort. We are also evaluating a number of secondary and additional endpoints to support maralixibat's effect on the underlying disease. These additional endpoints include the mean change in pruritus frequency, the mean change in sBA, mean change in quality of life as measured by the PedsQL and the proportion of patients who experience an improvement from baseline in height z-score. We expect to report topline data from the Phase 3 MARCH clinical trial in early 2022. We expect that the data from our Phase 3 MARCH clinical trial, if positive, together with natural history data set comparisons and the data from the Phase 2 INDIGO clinical trial, will form the basis for our planned NDA submission to the FDA for maralixibat in PFIC.



Safety and Tolerability Data for Maralixibat

In the ALGS clinical development program, which includes five clinical trials comprising 86 patients up to 21 years of age, patients received doses of maralixibat up to 760 µg/kg per day. In a pooled analysis, the most common ($\geq 5\%$) adverse reactions of any grade were diarrhea and abdominal pain, which were mostly mild to moderate in severity and resolved during continued maralixibat treatment. No patients discontinued maralixibat due to these adverse reactions. A summary of placebo comparisons from the ICONIC clinical trial and a pooled analysis of ITCH and IMAGO clinical trials in ALGS are provided below.

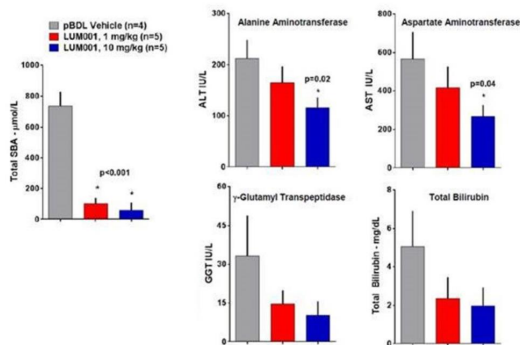
Number of participants, n (%)	ICONIC					ITCH & IMAGO	
	Week 0–18 (N = 31)	Week 19-22 Maralixibat (n = 13)	Week 19-22 Placebo (n = 16)	Week 23–48 (N = 29)	Week 49+ (N = 29)	Baseline-week 13 Maralixibat (n = 39)	Baseline-week 13 Placebo (n = 18)
Any TEAE, n (%)	30 (97)	7 (54)	12 (75)	25 (86)	23 (79)	35 (90)	16 (89)
Grade 3 or 4 TEAE	6 (19)	0	1 (6)	2 (7)	6 (21)	2 (5)	2 (11)
Serious TEAE (all unrelated to maralixibat)	4 (13)	1 (8)	1 (6)	5 (17)	5 (17)	1 (3)	0
TEAE leading to study drug discontinuation	2 (7)	0	0	1 (3)	3 (10)	1 (3)	1 (6)
TEAE potentially related to study drug	12 (39)	1 (8)	3 (19)	1 (3)	7 (24)	27 (69)	11 (61)
Gastrointestinal disorders	22 (71)	2 (15)	3 (19)	14 (48)	16 (55)	26 (67)	11 (61)
Diarrhea	13 (42)	1 (8)	1 (6)	5 (17)	8 (28)	17 (44)	8 (44)

Liver-related events were assessed in two maralixibat program-wide safety reviews, including two adjudications by independent groups of pediatric hepatologists and drug-induced liver injury experts in cholestatic indications. The independent expert group concluded that there was no serious concern for significant general or sporadic drug-induced liver injury. The analyses showed that maralixibat may cause isolated, asymptomatic and reversible ALT elevations in some participants with ALGS. However, there has been no serious adverse event (“SAE”) associated with these isolated ALT increases in participants with ALGS and no case of drug-induced liver injury or liver-related morbidity or mortality has been reported to date in over 1600 adult and pediatric study participants. There is evidence that these effects of ALT elevations are likely due to a mechanism related to the underlying disease rather than a direct hepatotoxic effect, as a similar degree of isolated ALT/AST increases are seen after PBD in patients with ALGS. In addition, these ALT/AST increases have not been observed in participants with PFIC exposed to maralixibat.

Maralixibat in BA

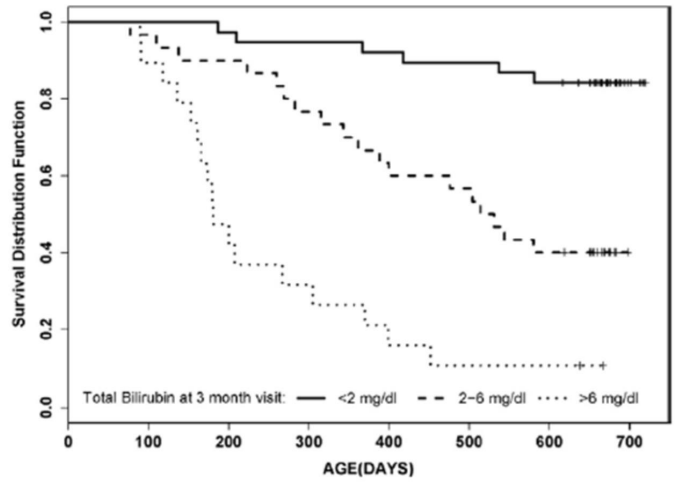
We believe ASBT inhibition has therapeutic potential in this patient population. This is based on analogous disease models, including rat partial bile duct ligation, that replicate the extra-hepatic cholestasis and liver injury associated with BA. As shown below, maralixibat alleviated BA biochemical and histological and dose-dependent changes in sBA and liver transaminases.

Maralixibat treatment reduces sBAs and liver injury at day 7 in bile duct ligated rats



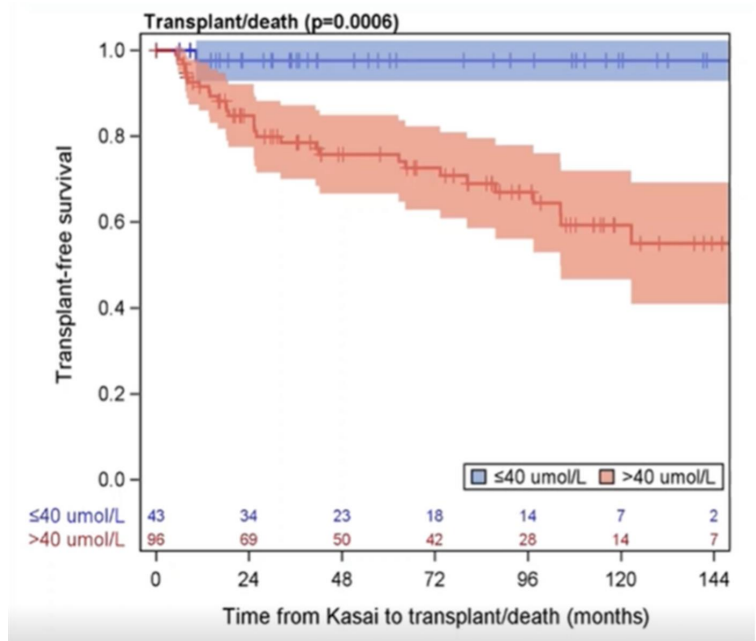
Bilirubin and sBA levels post-Kasai procedure have been associated with risk of progression to transplant as shown in the figures below:

Bilirubin levels post-Kasai procedure may predict future transplant



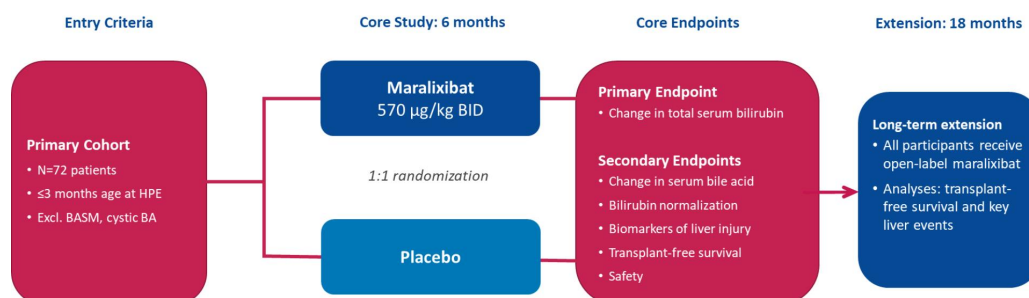
The figure above shows a Kaplan-Meier analysis of outcome based on total bilirubin levels three months after a Kasai procedure. At three months after the Kasai procedure, total bilirubin levels were < 2mg/dL in 38 children, between 2 and 6 mg/dL in 30 children and > 6mg/dL in 19 children.

sBA post-Kasai procedure may predict future transplant



The above Kaplan-Meier curve demonstrates a significantly improved transplant survival rate in patients with sBA levels $\leq 40 \mu\text{mol/L}$ at 6 months. Only 1 of 43 patients, with sBAs $\leq 40 \mu\text{mol/L}$ (as depicted by the blue line) required a liver transplant as compared to 31 of 96 infants requiring a transplant in those infants with sBAs $> 40 \mu\text{mol/L}$ (as depicted by the red line).

Based on these data, we designed the Phase 2 EMBARK clinical trial. The primary objective of the EMBARK clinical trial is to assess the safety and efficacy of maralixibat in infants with BA. The clinical trial will evaluate maralixibat's ability to reduce the amount of bile acids in the blood, helping to prevent liver damage and the need for future liver transplantation. As depicted in the figure below, EMBARK is a randomized, placebo-controlled clinical trial that will evaluate approximately 72 patients who have previously undergone a Kasai procedure. Patients will be randomized to receive maralixibat 570 $\mu\text{g/kg}$ BID or placebo for six months. The primary endpoint in the clinical trial is change in total serum bilirubin. Secondary endpoints include reduction in sBA, bilirubin normalization, biomarkers of liver injury, transplant-free survival, and safety. After the first six months of evaluation, all patients will receive maralixibat in an open-label long-term extension with the goal of assessing transplant-free survival and key liver events.



Overview of Volixibat

Our second product candidate, volixibat, is a novel, oral, minimally-absorbed agent designed to selectively inhibit ASBT. We believe that volixibat may offer a novel approach in the treatment of adult cholestatic diseases by blocking recycling of bile acids, thereby reducing bile acids systemically and in the liver. Phase 1 and Phase 2 clinical trials of volixibat demonstrated decreases in LDL cholesterol, increases in $7\alpha\text{C4}$ and increases in fecal bile acid content, all markers of ASBT inhibition.

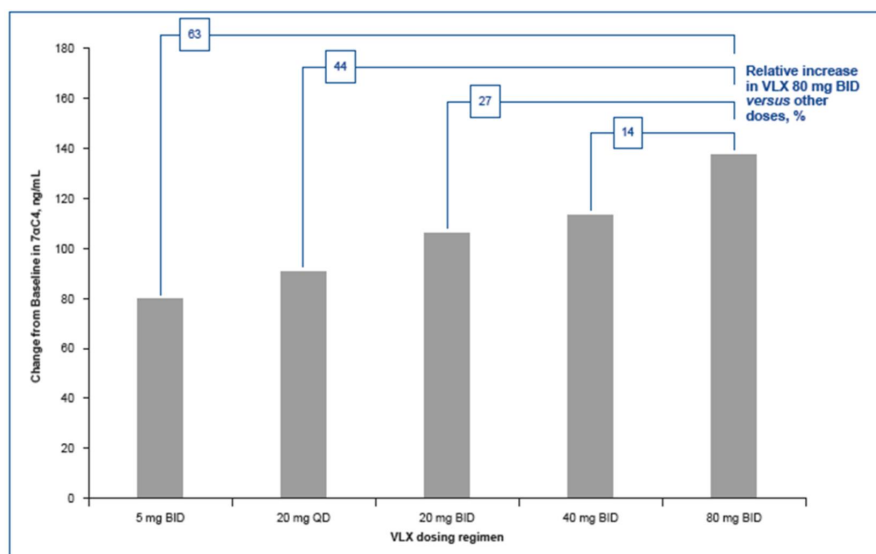
Development of Volixibat

Volixibat has been evaluated in over 400 subjects across multiple clinical trials. In Phase 1 clinical trials in 92 healthy volunteers, volixibat was generally well tolerated. The most common adverse events reported were mild to moderate GI events observed in the volixibat groups. The only treatment-related SAE reported was one event of elevated ALT. Volixibat was also found to decrease cholesterol levels in healthy subjects, consistent with its mechanism of lowering bile acid levels. An additional Phase 1 clinical trial was conducted in obese and overweight, but otherwise healthy, adults to evaluate volixibat's potential to lower bile acid levels by measuring the excretion of bile acids in the feces. This clinical trial indicated volixibat increased fecal bile acid levels in a dose dependent manner, but without appreciable change in GI tolerability at higher doses.

Volixibat was also studied in a multicenter, Phase 2, double-blind, randomized, placebo-controlled NASH clinical trial. 196 participants were randomized to receive oral placebo or volixibat in doses of 5 mg, 10 mg or 20 mg QD for 48 weeks. The safety results were consistent with prior clinical trials of volixibat. In a planned interim analysis, there was no difference between volixibat and placebo treated groups on magnetic resonance imaging-derived proton density fat fraction. Volixibat was associated with lower LDL cholesterol and increased $7\alpha\text{C4}$, indicative of ASBT inhibition. After the interim analysis, Shire plc discontinued the development of volixibat for the treatment of NASH. Based on these results, we plan to pursue the development of volixibat for the treatment of adult cholestatic liver diseases.

Phase 1 Dose Ranging Clinical Trial

A single-center, placebo-controlled, single-blind, multiple-dose/regimen, parallel-group, dose-finding clinical trial in healthy adults was completed in 2020. This clinical trial was designed to evaluate the effect of a range of volixibat QD or BID dose regimens versus placebo on fecal bile acid excretion. Participants were randomized to one of five cohort groups to receive either volixibat 5 mg twice daily (BID), volixibat 20 mg QD, volixibat 20 mg BID, volixibat 40 mg BID, or volixibat 80 mg BID, and each cohort underwent four treatment periods. Volixibat was well tolerated and all BID doses increased fecal bile acid excretion versus QD, and higher doses increased bile acid synthesis as demonstrated by increased $7\alpha\text{C}_4$. Based on the $7\alpha\text{C}_4$ and fBA activity levels shown in these results, doses of 20 mg and 80 mg BID are being evaluated in our registrational programs.



*Baseline for fBA was defined as Day 5. Thus, the summary represents the data at 7 days after Baseline
 $7\alpha\text{C}_4$, 7 alpha-hydroxy-4-cholesten-3-one; BID, twice daily; fBA, fecal bile acid; QD, once daily; VLX, volixibat

On-going and Future Clinical Development of Volixibat

We are evaluating the utility of volixibat in adult cholestatic liver diseases and initiated clinical trials in PSC and ICP in the first quarter of 2021. Additionally, we plan to start a clinical trial in PBC in the second half of 2021.

Phase 2a/2b OHANA Trial in ICP

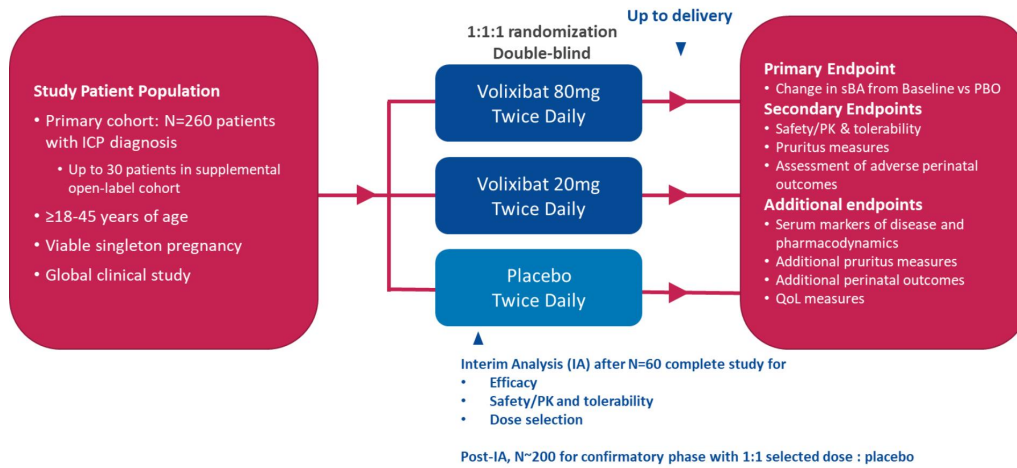
In ICP, we are evaluating the potential of volixibat to lower sBA levels in patients with elevated sBA levels, who are considered at high risk of preterm labor, stillbirth or other perinatal complications.

As depicted in the figure below, the OHANA phase 2a/2b clinical trial is evaluating two doses of volixibat compared to placebo.

The OHANA clinical trial primary cohort will evaluate approximately 260 patients who have been diagnosed with ICP and have elevated sBA levels consistent with at least moderate ICP. Additionally, up to 30 participants with a lower threshold, yet still elevated, sBA levels, consistent with mild ICP will be enrolled into an open-label supplemental cohort.

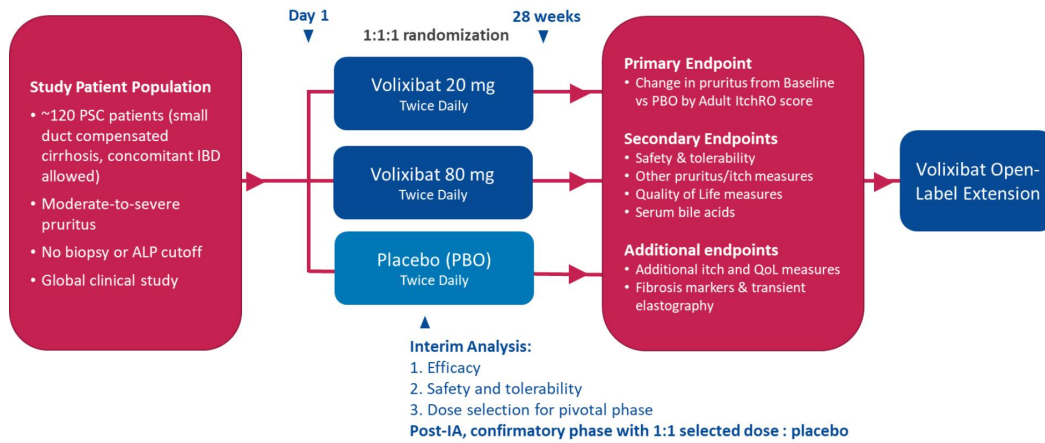
Patients in the clinical trial are randomized to receive either volixibat 80 mg BID or 20 mg BID, or placebo BID up to delivery of their baby. The primary endpoint will assess the mean change from baseline in total sBA

concentration as compared to placebo. Secondary endpoints will assess pruritus improvements, adverse perinatal outcomes, safety, tolerability, and other measures.



Phase 2b VISTAS Trial in PSC

In PSC, based on the reductions in pruritus observed in PSC patients receiving maralixibat, we are conducting a Phase 2b clinical trial of volixibat in PSC patients with pruritus. The VISTAS clinical trial will evaluate approximately 120 patients with pruritus due to PSC and will include an adaptive interim analysis. After the interim analysis, the confirmatory phase of VISTAS will evaluate a single dose of volixibat compared to placebo. In addition to the 28-week primary analysis, patients will be eligible to continue on open label volixibat treatment and will be evaluated for durability of response and changes in fibrosis markers.



Phase 2b Clinical Trial in PBC

We are currently planning to initiate a Phase 2b clinical trial of volixibat in PBC in the second half of 2021. We are designing the program to focus on the treatment of cholestatic pruritus with elevated or normal alkaline phosphatase.

License, Finance and Royalty Agreements

Assignment and License Agreement with Shire International GmbH (Takeda)

In November 2018, we entered into an assignment and license agreement (“Shire License Agreement”) with Shire International GmbH (“Shire”), which was subsequently acquired by Takeda Pharmaceutical Company Limited. Pursuant to the Shire License Agreement, Shire assigned, transferred and conveyed all of its right, title and interest in and to the Pfizer Agreement, Satiogen Agreement and Sanofi Agreement, each of which is defined below.

In addition, Shire granted us an exclusive, royalty bearing, sublicensable, worldwide license under certain regulatory materials as well as patents and know-how, which we refer to collectively as the Shire IP, relating to the maralixibat compound and the volixibat compound in development by Shire as of that date, which we collectively refer to as the Shire Licensed Products, to develop, have developed, make, have made, use, sell, have sold, offer for sale or import the Shire Licensed Products worldwide for the therapeutic or prophylactic application in human health. We have sole authority and responsibility over development and commercialization activities for the Shire Licensed Products, and we are required to use commercially reasonable efforts to perform certain development, regulatory and commercialization activities with respect to the PFIC, ALGS and BA indications for maralixibat and unspecified indications with respect to volixibat. We will solely own all inventions and discoveries arising out of activities conducted by us under the Shire License Agreement. We will also be responsible for the preparation, filing, prosecution and maintenance of patents under the Shire License Agreement and the cost thereof. We have the first right, but are not obligated, to enforce any patent licensed under the Shire License Agreement.

As consideration for the rights granted to us under the Shire License Agreement, we made a one-time upfront payment to Shire of \$7.5 million and issued Shire 1,859,151 shares of our common stock pursuant to a common stock issuance agreement that we entered into concurrently with the Shire License Agreement. We paid a \$2.5 million milestone payment to Shire as a result of the initiation of the Phase 3 MARCH clinical trial in July 2019.

We are also required to pay Shire up to an aggregate of \$107.0 million upon the achievement of certain other clinical development and regulatory milestones for maralixibat in the PFIC, ALGS and BA indications, and a \$25.0 million payment upon regulatory approval of maralixibat for each and every other indication. Each such milestone payment will be paid only once for each such indication during the term of the Shire License Agreement, the first time maralixibat reaches such milestone event, regardless of the number of times such milestone is reached by maralixibat for the same indication. In addition, we are required to pay up to an aggregate of \$30.0 million upon the achievement of certain clinical development and regulatory milestones for volixibat solely for the first indication sought. Each such milestone payment will be paid only once for the first indication for which volixibat is developed during the term of the Shire License Agreement, the first time volixibat reaches such milestone event, regardless of the number of products or the number of indications for which volixibat is developed.

In July 2019, we achieved a development milestone under the Shire License Agreement related to the initiation of the Phase 3 MARCH clinical trial and made a \$2.5 million payment to Shire and a \$0.5 million payment to Satiogen accordingly. In December 2020, we achieved a further development milestone related to the submission of the MAA for maralixibat for the treatment of PFIC2 and made a \$10.0 million payment to Shire. In January 2021 we achieved a development milestone related to volixibat and made a \$2.0 million payment to Shire.

Upon achievement of certain thresholds for aggregate worldwide net sales for all Shire Licensed Products, we are required to pay Shire, on a one-time, non-refundable and non-creditable basis, up to an aggregate of \$30.0 million in tiered sales milestone payments. Lastly, upon certain annual worldwide net sales of all Shire Licensed Products, we are required to pay Shire, on a non-refundable and non-creditable basis, tiered royalties with rates ranging from low double-digits to mid-teens (“Shire royalties”). If we actually make royalty payments to

Sanofi, which is defined below, under the Sanofi Agreement, the Shire royalties will be reduced by low to high single digit percentages of certain net sales thresholds. Similarly, if we actually make royalty payments to Satiogen, which is defined below, under the Satiogen Agreement, the Shire royalties will be reduced by a low single digit percentage of net sales.

Under the Shire License Agreement, we are prohibited from developing any competing product prior to the five year anniversary of the first commercial sale of a Shire Licensed Product, or commercializing any competing product prior to the eight year anniversary of the first commercial sale of a Shire Licensed Product. For purposes of the Shire License Agreement, a competing product is any product that is or contains a compound (A) where the primary method of action is ASBT inhibition activity or (B) that is commercialized or developed for any PFIC, ALGS, or BA indication, except (B) shall not apply with respect to (1) a given indication if a product failure has occurred with respect to such indication (e.g., if a product failure has occurred for a Shire Licensed Product for the BA indication, we may thereafter develop and commercialize a product for the BA indication if such product uses a different primary method of action than ASBT inhibition activity) or (2) a given product if such product is a product that is not deleterious to the sales or pricing of a Shire Licensed Product.

The Shire License Agreement will remain in effect on a country-by-country and Shire Licensed Product-by-Shire Licensed Product basis and will continue on such basis until the later of the (i) expiration of the last patent or patent application licensed under the Shire License Agreement that covers a Shire Licensed Product, (ii) expiration of any regulatory exclusivity period, and (iii) tenth anniversary of the first commercial sale of such Shire Licensed Product in such country. The term of the last patent or patent application licensed under the Shire License Agreement ends on October 26, 2032, absent patent term adjustment or extension. After November 5, 2021, we may unilaterally terminate the Shire License Agreement for any reason or no reason upon 90 days' written notice to Shire. In addition, we may also terminate the Shire License Agreement if we reasonably determine that we are precluded from further development due to materially adverse pre-clinical or clinical pathology or toxicology data. Either party may terminate the Shire License Agreement in the event of the other party's insolvency or for the other party's material breach of the Shire License Agreement that remains uncured after 90 days of receiving written notice of such breach. Shire may terminate the Shire License Agreement upon our or our affiliates' challenge to the validity of the patents licensed under the Shire License Agreement.

License Agreement with Pfizer Inc.

Through the Shire License Agreement, we were assigned the rights to the license agreement ("Pfizer Agreement"), with Pfizer Inc. ("Pfizer"), pursuant to which we obtained an exclusive, worldwide license to Pfizer's know-how related to maralixibat, or the Pfizer Know-How. Under the Pfizer Agreement, we are permitted to research, develop, manufacture and commercialize products utilizing the Pfizer Know-How for the diagnosis, treatment, prevention, mitigation and cure of human diseases and disorders, and to sublicense such rights. Pfizer retained the right to use the Pfizer Know-How to conduct internal research and to use a third party to conduct research on Pfizer's behalf.

We have sole responsibility and control over development and commercialization activities for the Pfizer Know-How and products utilizing the Pfizer Know-How, and we are obligated to use commercially reasonable efforts to develop and commercialize products utilizing the Pfizer Know-How. In the event we determine to sublicense to a third party our right to commercialize the Pfizer Know-How or products utilizing the Pfizer Know-How under the Pfizer Agreement, Pfizer has the first right to negotiate such a commercial license with us.

Ownership of inventions and discoveries under the Pfizer Agreement will be determined in accordance with the rules of inventorship under United States patent laws. We will own and bear all expenses incurred in preparing, filing, prosecuting and maintaining all patents for inventions that are solely invented by us.

As consideration, upon commercialization of any product utilizing the Pfizer Know-How, we will be required to pay to Pfizer a low single-digit royalty on net sales of such products sold by us, our affiliates or sublicensees. Our royalty obligations continue on a licensed product-by-licensed product basis until the eighth anniversary of the first commercial sale of such licensed product anywhere in the world.

We may unilaterally terminate the Pfizer Agreement for any reason or no reason upon 90 days' written notice to Pfizer. Either party may terminate the Pfizer Agreement in the event of the other party's insolvency or for the other party's material breach of the Pfizer Agreement which remains uncured after 60 days of receiving written notice of such breach, or 30 days in the case of a payment breach. Absent early termination, the Pfizer Agreement will automatically expire on a country-by-country basis upon the expiration of our royalty payment obligations.

License Agreement with Sanofi-Aventis Deutschland GmbH

Through the Shire License Agreement, we were assigned the rights to the license agreement, as amended ("Sanofi Agreement"), with Sanofi-Aventis Deutschland GmbH ("Sanofi"), under which we obtained an exclusive, worldwide license to certain patents and know-how controlled by Sanofi related to volixibat ("Sanofi Technology"). Under the Sanofi Agreement, we are permitted to develop and commercialize products containing volixibat utilizing the Sanofi Technology. Additionally, under the Sanofi Agreement, we are permitted to manufacture products containing volixibat utilizing the Sanofi Technology and to sublicense such rights. In addition, Sanofi granted to us, under certain conditions, an exclusive option to obtain an exclusive license to manufacture volixibat during the term of the Sanofi Agreement. We exercised this option in May 2020 and are transferring manufacturing of volixibat to a third-party contract manufacturer. Sanofi retained the right to practice the Sanofi Technology outside the scope of the license granted to us under the Sanofi Agreement and to make and use for internal research purposes, provided that upon our request, Sanofi is obligated to provide us with a written summary of the results of any such research to the extent such results relate to the use of volixibat as an ASBTi.

Under the Sanofi Agreement, we have sole authority and responsibility over development and commercialization activities for licensed products, and we are required to use diligent efforts to perform certain development, regulatory and commercialization activities.

With the exception of Sanofi's rights on its further optimization of the process of manufacturing of the product utilizing the Sanofi Technology, we will own all inventions and discoveries arising out of activities conducted by us under the Sanofi Agreement and we will be responsible for the preparation, filing, prosecution and maintenance of patents under the Sanofi Agreement. Further, we will have the first right, but will not be obligated, to enforce patents under the Sanofi Agreement. If we do not exercise our right to enforce patents under the Sanofi Agreement, Sanofi will be able to enforce the patents.

We are required to pay to Sanofi up to an aggregate of \$36.0 million upon the achievement of certain regulatory, commercialization and product sales milestones. Upon commercialization of any product utilizing the Sanofi Technology, we will be required to pay to Sanofi tiered royalties in the mid to high single-digit range based upon net sales of licensed products sold by us and our affiliates and sublicensees in a calendar year, subject to adjustments in certain circumstances. Our royalty obligations continue on a licensed product-by-licensed product and country-by-country basis until the later to occur of the expiration of the last valid claim in a licensed patent or patent application covering the applicable licensed product in such country and ten years after the first commercial sale of a licensed product following regulatory approval in such country. The term of the last patent or patent application licensed under the Sanofi Agreement ends on May 26, 2030, absent patent term adjustment or extension. In the event we sublicense our right to commercialize a product utilizing the Sanofi Technology, we are obligated to pay to Sanofi a fee based on a percentage of sublicense fees received by us, which percentage ranges from the mid-teens to low-thirties, depending on the stage of development of such licensed product, and is subject to adjustment in certain circumstances.

For three years after the first commercial sale of a product utilizing the Sanofi Technology, on a licensed product-by-licensed product basis, we may not, through our own efforts or with an affiliate or third party, commercialize any product for specified indications with a method of action that reduces the reabsorption of bile acids in the intestinal tract, except for the commercialization of products utilizing the Sanofi Technology under the Sanofi Agreement.

We may unilaterally terminate the Sanofi Agreement for any reason or no reason upon 60 days' written notice to Sanofi after the second anniversary of the Sanofi Agreement. We may also terminate the Sanofi Agreement on a country-by-country or licensed product-by-licensed product basis upon written notice to Sanofi (1) if we reasonably determine that we are precluded from proceeding with the first Phase 2b clinical trial for a product utilizing the

Sanofi Technology in certain major markets due to certain safety failures or (2) after using diligent efforts, we reasonably determine that we are precluded from proceeding with a Phase 3 clinical trial for a product utilizing the Sanofi Technology in certain major markets due to certain safety or efficacy failures. Either party may terminate the Sanofi Agreement in the event of the other party's insolvency or for the other party's material breach of the Sanofi Agreement which remains uncured after 90 days of receiving written notice of such breach, or ten business days in the case of a payment breach. Absent early termination, the Sanofi Agreement will remain in effect on a country-by-country and licensed product-by-licensed product basis until the expiration of our royalty payment obligations for such licensed product in such country.

License Agreement with Satiogen Pharmaceuticals, Inc.

Through the Shire License Agreement, we were assigned the rights to the license agreement, as amended ("Satiogen Agreement"), with Satiogen Pharmaceuticals, Inc ("Satiogen"), under which we obtained an exclusive, worldwide license to certain patents and know-how controlled by Satiogen related to ASBTis ("ASBTi Technology"), and TGR5 agonists ("TGR5 Technology"). Under the Satiogen Agreement, we are permitted to develop, manufacture and commercialize products utilizing the ASBTi Technology or TGR5 Technology for the diagnosis, treatment, prevention, mitigation and cure of human diseases and disorders, other than diabetes, obesity or a combination thereof, and to sublicense such rights.

We have sole responsibility and control over development and commercialization activities for products utilizing the ASBTi Technology or TGR5 Technology under the Satiogen Agreement and we are required to use commercially reasonable efforts to develop and commercialize such licensed products.

Ownership of inventions and discoveries conceived or reduced to practice under the Satiogen Agreement will be determined in accordance with the rules of inventorship under United States patent laws. We will own any and all inventions made by us or jointly with Satiogen under the Satiogen Agreement and we will be responsible for filing, prosecuting and maintaining any patents for such inventions. Satiogen will own any and all inventions that are solely invented by Satiogen under the Satiogen Agreement and will be responsible for preparing, filing, prosecuting and maintaining any patents for such inventions. Satiogen will be responsible for filing, prosecuting and maintaining patents related to the ASBTi Technology and TGR5 Technology controlled by Satiogen as of the effective date or during the term of the Satiogen Agreement. Additionally, prior to certain events specified in the Satiogen Agreement, Satiogen will have the sole right, but not the obligation, to enforce patents related to the ASBTi Technology and the TGR5 Technology; after which, we will have the sole right, but not the obligation, to enforce patents related to the ASBTi Technology and the TGR5 Technology. In March 2017, the Satiogen Agreement was amended to terminate the license of certain patents related to the ASBTi Technology and TGR5 Technology as each relates to diabetes and obesity.

We are required to pay to Satiogen up to an aggregate of \$10.5 million upon the achievement of certain milestones, of which \$0.5 million relates to the initiation of certain development activities, \$5.0 million relates to the completion of regulatory approvals and \$5.0 million relates to commercialization activities. We will be required to pay to Satiogen a low single-digit royalty on net sales of products utilizing the ASBTi Technology or TGR5 Technology sold by us and our affiliates. Our royalty obligations continue on a licensed product-by-licensed product and country-by-country basis until the expiration of the last valid claim in a licensed patent or patent application covering the applicable licensed product in such country. The term of the last patent or patent application licensed under the Satiogen Agreement ends on August 30, 2031, absent patent term adjustment or extension.

In the event we sublicense any of our rights under the ASBTi Technology or TGR5 Technology to a third party, we are obligated under the Satiogen Agreement to pay to Satiogen a fee based on a percentage of sublicense revenue received by us, which percentage ranges from the mid-teens to mid-twenties, depending on whether the right granted is in connection with the ASBTi Technology or TGR5 Technology, and the stage of development of such sublicensed technology. In addition, we are obligated under the Satiogen Agreement to pay to Satiogen a percentage of royalties we receive in consideration for the grant of such sublicense based on a percentage of revenue generated by such sublicensee for sales of products utilizing the ASBTi Technology or TGR5 Technology, which percentage is in the low-fifties and is subject to adjustment in certain circumstances. This payment will not exceed an amount that is one-half of our low single-digit royalty obligation to Satiogen.

We may unilaterally terminate the Satiogen Agreement for any reason or no reason upon 90 days' written notice to Satiogen. If we cease all research, development and commercialization efforts with respect to all licensed products related to the ASBTi Technology or the TGR5 Technology for over one year, or we determine to cease all such efforts, Satiogen may elect to terminate the Satiogen Agreement with respect to the license under the ASBTi Technology or the TGR5 Technology, respectively. Either party may terminate the Satiogen Agreement for the other party's material breach of the Satiogen Agreement which remains uncured after 90 days of receiving written notice of such breach. Absent early termination, the Satiogen Agreement will automatically terminate upon the expiration of our royalty obligations.

Revenue Interest Purchase Agreement with Oberland

In December 2020, we entered into a Revenue Interest Purchase Agreement ("RIPA") with Mulholland SA LLC, an affiliate of Oberland Capital LLC, as agent for the purchasers party thereto (the "Purchasers"), and the Purchasers. Pursuant to the RIPA, the Purchasers paid us \$50.0 million on closing, less certain issuance costs. We may also be entitled to receive up to approximately \$150.0 million in subsequent installments as follows: (i) \$65.0 million if the FDA has accepted for review our NDA for maralixibat as a treatment for cholestatic pruritus in patients with ALGS on or prior to a specified date; (ii) \$35.0 million if the FDA has approved maralixibat as a treatment for ALGS on or prior to a specified date; and (iii) up to \$50.0 million at the option of the Purchasers to finance in-licenses or other acquisitions.

As consideration for such payments, the Purchasers will have a right to receive certain revenue interests (the "Revenue Interests") from us based on annual net sales of maralixibat, if approved, which will be tiered payments (the "Revenue Interest Payments") based on whether such annual net sales are (i) less than or equal to \$350.0 million ("Tier 1"), (ii) exceeding \$350.0 million and less than or equal to \$1.1 billion ("Tier 2"), or (iii) exceeding \$1.1 billion ("Tier 3"). The Revenue Interest Payments will initially be 9.75% (at Tier 1) and 2.00% (at Tier 2 and Tier 3) of such annual net sales in a specified territory (the "Covered Territory"); provided that (i) if the Purchasers have received Revenue Interest Payments in an amount equal to or greater than 110.0% of the total payments actually made by the Purchasers to us, exclusive of transaction expenses (the "Cumulative Purchaser Payments"), on or prior to December 31, 2026, the Revenue Interests shall be reduced to 2.00% at Tier 1 and 0.00% at Tier 3 for all subsequent calendar years beginning on January 1, 2027 and (ii) if the Purchasers have not received Revenue Interest Payments in an amount equal to or greater than 110.0% of the Cumulative Purchaser Payments on or prior to December 31, 2026, the Revenue Interests shall be increased for all subsequent calendar years beginning on January 1, 2027 to a single defined rate (with no separate tiers) that would have provided the Purchasers with an amount equal to 110.0% of the Cumulative Purchaser Payments on or prior to December 31, 2026 had such rate applied to Tier 1 of initial Revenue Interest Payments. The Purchasers' rights to receive the Revenue Interest Payments shall terminate on the date on which the Purchasers have received Revenue Interest Payments of 195.0% of the Cumulative Purchaser Payments, unless the RIPA is terminated earlier.

Intellectual Property

Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates and other discoveries, inventions, trade secrets and know-how that are critical to our business operations. Our success also depends in part on our ability to operate without infringing the proprietary rights of others, and in part, on our ability to prevent others from infringing our proprietary rights. A comprehensive discussion on risks relating to intellectual property is provided under "Risk Factors" under the subsection "Risks Related to Our Intellectual Property."

We have developed and continue to develop patent portfolios around our product candidates, maralixibat and volixibat. We have rights to pending patent applications in the United States, Europe, South Korea, Israel, Hong Kong and Singapore covering the methods of treating cholestasis using ASBTis that have limited systemic exposure, which, if issued, would expire in October 2032, absent any patent term adjustments or extensions. We have rights to an issued patent in the United States directed to treating or ameliorating PFIC2 in a pediatric subject comprising administering maralixibat, which expires in October 2032. We have rights to granted and/or issued patents in Australia, Brazil, Canada, China, Japan, Mexico, South Korea, Armenia, Azerbaijan, Belarus, Kazakhstan, Kyrgyzstan, Russia, Tajikistan, Turkmenistan, South Africa and Macau covering the methods of treating cholestasis using ASBTis that have limited systemic exposure, which expire in October 2032. We also have rights to pending

patent applications in United States, Europe, Australia, Japan, Eurasia, South Korea, Mexico, Hong Kong, Singapore and South Africa, covering methods of treating pediatric cholestatic liver diseases using ASBTis that have limited systemic exposure, which, if issued, would expire in October 2032, absent any patent term adjustments or extensions. We have rights to granted and/or issued patents in Australia, Brazil, Canada, China, Israel, Japan, Mexico, South Korea, South Africa, Singapore, Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Ireland, Italy, Netherlands, Norway, Poland, Portugal, Slovak Republic, Spain, Sweden, Switzerland, United Kingdom, Armenia, Azerbaijan, Belarus, Kazakhstan, Kyrgyzstan, Russia, Tajikistan, Macau and Turkmenistan covering methods of treating pediatric cholestatic liver diseases using ASBTis that have limited systemic exposure, which expire in October 2032. We also have rights to a granted patent in South Africa covering pediatric dosage forms of ASBTis that have limited systemic exposure, which expires in October 2032. We also have rights to a pending patent application in China covering pediatric dosage forms of ASBTis that have limited systemic exposure, which, if issued, would expire in October 2032, absent any patent term adjustments or extensions. We have rights to a pending Patent Cooperation Treaty (“PCT”) application directed to methods for modulating a dosage of an ASBTi and to methods for using patient genotype to predict response to ASBTi administration in patients with BSEP deficiency. We have rights to a pending PCT application and pending United States applications directed to methods for treating cholestatic liver disease comprising administering higher dosages of ASBTis. We have rights to a pending PCT application directed to methods of increasing growth in pediatric subjects having cholestatic liver disease by administering ASBTis. Any patents issuing from these PCT or United States applications would expire in 2040, absent any patent term adjustments or extensions. We have licensed patent applications in the United States and Europe from Satiogen covering therapeutic uses of ASBTis that have limited systemic exposure for treating inflammatory intestinal conditions, which, if issued, would expire in May 2031, absent any patent term adjustments or extensions. One of these Satiogen applications recently issued as United States Patent No. 10,251,880. We have licensed an issued United States patent, as well as issued foreign counterparts in Argentina, Austria, Australia, Belgium, Canada, Switzerland, China, Germany, Denmark, Spain, Finland, France, United Kingdom, Greece, Hong Kong, Ireland, Israel, India, Italy, Japan, South Korea, Liechtenstein, Mexico, Malaysia, Netherlands, Norway, Portugal, Russia, Sweden, Singapore, Taiwan and Turkey, and a pending counterpart in Brazil from Sanofi, that cover the composition and methods of making volixibat and salts thereof, expiring in December 2027. Patents related to maralixibat and volixibat may be eligible for patent term extensions in certain jurisdictions, including the United States and Europe, upon approval of a commercial use of the corresponding product by a regulatory agency in the jurisdiction where the patent was granted and/or issued.

We do not have patents or patent applications covering maralixibat as a composition of matter. Therefore, the primary patent-based intellectual property protection for our maralixibat program will be any patents granted on the pending method-of-use and dosage form patent applications.

In addition to patent protection, we rely on trade secret protection, trademark protection and know-how to expand our proprietary position around our chemistry, technology and other discoveries and inventions that we consider important to our business. We are a party to a number of license agreements under which we are granted intellectual property rights to know-how that are important to our business. We have licensed know-how related to maralixibat in the United States, Europe and other countries from Pfizer. We have licensed know-how related to ASBTi Technology and TGR5 Technology from Satiogen. We have licensed know-how related to volixibat from Sanofi. Our existing license agreements as related to maralixibat and volixibat impose various development, regulatory and/ commercial diligence obligations, payment of milestones and/or royalties and other obligations.

In addition, we currently have orphan drug designation for maralixibat for the treatment of ALGS, PFIC, PSC and PBC in the United States and the European Union, providing the opportunity to receive seven years of market exclusivity in the United States, which can be extended to seven and a half years if trials are conducted in accordance with an agreed-upon pediatric investigational plan, and ten years of market exclusivity in the European Union, which can be extended to 12 years in the European Union if trials are conducted in accordance with an agreed-upon pediatric investigational plan.

Upon approval in the United States, as neither maralixibat or volixibat has previously been approved in the United States for any indication, both product candidates may be eligible for five years of new chemical entity exclusivity, which would run currently with their seven years of orphan drug exclusivity if we obtain orphan drug exclusivity for their approved uses.

We also seek to protect our intellectual property in part by entering into confidentiality agreements with companies with whom we share proprietary and confidential information in the course of business discussions, and by having confidentiality terms in our agreements with our employees, consultants, scientific advisors, clinical investigators and other contractors and also by requiring our employees, commercial contractors, and certain consultants and investigators, to enter into invention assignment agreements that grant us ownership of any discoveries or inventions made by them while in our employ.

Furthermore, we seek trademark protection in the United States and internationally where available and when we deem appropriate.

Sales and Marketing

We currently have a limited commercial organization. We are in the process of building the commercial infrastructure necessary to effectively support the commercialization of maralixibat and volixibat, if approved, in North America and Europe and we may decide to use strategic partners, distributors, or contract management organizations to assist in the commercialization of maralixibat and volixibat in other markets. We believe that our commercial organization can be targeted to the relatively small number of specialists who treat patients with pediatric cholestasis, such as ALGS, PFIC and BA.

The commercial infrastructure for orphan products typically consists of a targeted, specialty sales force that calls on a limited and focused group of physicians supported by sales management, internal sales support, an internal marketing group and distribution support. Additional capabilities important to the marketplace include the management of key accounts such as managed care organizations, group-purchasing organizations, specialty pharmacies, government accounts and reimbursement support. Based on the number of physicians that treat cholestatic liver diseases, we believe that we can effectively target the relevant audience for maralixibat and volixibat in North America and Europe primarily through an internal sales force. To develop the appropriate commercial infrastructure, we will have to invest significant amounts of financial and management resources, some of which will be committed prior to any confirmation that maralixibat or volixibat will be approved.

In addition, we are building a medical affairs organization and multiple capabilities across North America and Europe to meet the scientific and medical educational needs of the healthcare providers and patients in the rare liver disease community, focusing on providing accurate disease state and balanced product information for appropriate management of patients with rare liver disorders. Medical affairs is comprised of medical information, patient advocacy, patient diagnosis, medical science liaisons, research and educational grants.

In October 2020, we entered into a services agreement with Eversana, a leading provider of commercial support services to the life science industry, to provide integrated nationwide distribution, specialty pharmacy, medical information, patient services and hub support for maralixibat in the United States, if approved.

Manufacturing

We do not own or operate manufacturing facilities for the production of maralixibat and volixibat or other product candidates that we may develop, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We currently depend on third-party contract manufacturers for all of our required raw materials, active pharmaceutical ingredient and finished products. Over the course of the development of our ASBTis we have used and continue to use multiple third-party contract manufacturers. We do not have any current contractual arrangements for the manufacture of commercial supplies of maralixibat or volixibat. Prior to our receipt of any approval from the FDA, if at all, we intend to enter into agreements for commercial production of our product candidates with third party suppliers. We currently employ internal resources and third-party consultants to manage our manufacturing contractors.

Competition

The biotechnology and pharmaceutical industries are subject to rapid and intense technological change. We face, and will continue to face, competition in the development and marketing of our products and product candidates from academic institutions, government agencies, research institutions and biotechnology and

pharmaceutical companies. Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approval and marketing than we do.

Competition may also arise from, among other things, new drug development technologies, new or improved treatment options for preventing or reducing the incidence of disease in diseases our products treat and new small molecule or other classes of therapeutic agents. Such developments by competitors could reduce or eliminate the use of our products or may limit the utility and application of ongoing clinical trials for our product candidates.

There are no FDA-approved therapies for the treatment of ALGS, PFIC, BA, PSC or ICP in the United States. Symptomatic treatment with antipruritics, such as cholestyramine, typically provides only modest relief. Bristol Myers Squibb Company has discontinued its brand name cholestyramine, but generic versions of the drug are marketed by Upsher-Smith Laboratories, Inc., Par Pharmaceutical Companies, Inc., Sandoz Inc., the generic pharmaceuticals division of Novartis AG and others. UDCA, as ursodiol, is marketed by a number of generic pharmaceutical companies such as Mylan Inc., Actavis Inc., Lannett Company, Inc. and Par Pharmaceutical Companies, Inc.

A number of drugs, including UDCA, rifampin and naltrexone, are used off-label to treat patients suffering from cholestatic liver diseases. Additionally, surgical interventions, such as partial external biliary diversion and nasobiliary drainage, and extracorporeal liver support, such as Molecular Adsorbent Recirculation System, are also employed in an attempt to lower bile acid levels, manage pruritus and improve measures of liver function.

We are aware of two other companies pursuing clinical development of therapies that reduce sBA levels via the ASBT pathway. GlaxoSmithKline plc and Albireo Pharma, Inc. (“Albireo”) have ASBTis in clinical development for cholestatic liver diseases. We are aware that Albireo has announced topline results from a Phase 3 trial for PFIC1 and PFIC2 patients for odevixibat and has an extension study and an expanded access program enrolling PFIC patients. Albireo’s NDA for odevixibat for the treatment of pruritus in patients with PFIC has been accepted by the FDA. Additionally, we are aware that Albireo has submitted an MAA for odevixibat. Albireo has also announced the initiation of studies of odevixibat in BA and ALGS and plans to pursue other cholestatic liver diseases. We are aware that GlaxoSmithKline plc has completed a Phase 2 trial of its ASBTi in PBC patients and has announced its intention to conduct a Phase 3 trial in PBC. We are also aware that Intercept Pharmaceuticals, Inc. is exploring BA as an indication for obeticholic acid. Further, we may compete with companies that are developing gene therapy for the treatment of PFIC. In adult settings of cholestasis, similar to pediatric settings, cholestyramine, UDCA, rifampin and naltrexone are commonly used agents. We are not aware of FDA approved therapeutics for the treatment of ICP or PSC. We are aware of several agents in clinical development for the treatment of PSC, including Cymabay’s seladelpar, DURECT Corporation’s DUR928, Gilead Sciences Inc.’s GS-9674, HighTide Biopharmaceutical Inc.’s HTD1801, Immunic Therapeutics’ IMU-838, Intercept’s Ocaliva, or obeticholic acid, NGM Biopharmaceuticals Inc.’s NGM282 and Pliant Therapeutics’ PLN-74809. Intercept Pharmaceuticals, Inc.’s Ocaliva is approved as a second-line treatment for PBC. We are aware of several agents in clinical development for the treatment of PBC including Cymabay’s seladelpar, Genfit’s elafibranor and NGM Biopharmaceuticals, Inc.’s NGM282. Furthermore, if approved, one of our own product candidates may be used off-label in the market for another of our product candidates, adversely affecting the sales of that product candidate.

Government Regulation and Product Approval

As a pharmaceutical company that operates in the United States, we are subject to extensive regulation. Government authorities in the United States (at the federal, state and local level) and in other countries extensively regulate, among other things, the research, development, testing, manufacturing, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug products such as those we are developing. Maralixibat and volixibat and any other product candidates that we develop must be approved by the FDA before they may be legally marketed in the United States and by the appropriate foreign regulatory agency before they may be legally marketed in foreign countries. Generally, our activities in other countries will be subject to regulation that is similar in nature and scope as that imposed in the United States, although there can be important differences. Additionally, some significant aspects of regulation in Europe are addressed in a centralized way, but country-specific regulation remains essential in many respects.

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act (“FDCA”), and implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. 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, among other actions, refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of extensive preclinical laboratory tests, preclinical animal studies and formulation studies in accordance with applicable regulations, including the FDA’s Good Laboratory Practice (“GLP”), regulations and other applicable regulations;
- submission to the FDA of an investigational new drug (“IND”), which must become effective before human clinical trials may begin;
- approval by an independent institutional review board (“IRB”), at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with applicable regulations, including the FDA’s good clinical practice (“GCP”), regulations to establish the safety and efficacy of the proposed drug for its proposed indication;
- submission to the FDA of an NDA for a new drug;
- satisfactory completion of an FDA advisory committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of an NDA to file the NDA for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with the FDA’s current good manufacturing practice (“cGMP”), requirements to assure that the facilities, methods and controls are adequate to preserve the drug’s identity, strength, quality and purity;
- potential FDA inspection of the preclinical and/or clinical trial sites that generated the data in support of the NDA; and
- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

Before testing any compounds with potential therapeutic value in humans, the drug 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 drug candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs. 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. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human trials. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance.

Clinical trials involve the administration of the drug candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

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

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

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

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA 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 trials may not be completed successfully within any specified period, if at all. The FDA, the IRB, or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug 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 drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

The results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. Data may come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational drug product to the satisfaction of the FDA. 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, the Pediatric Research Equity Act (“PREA”), requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation. Unless otherwise required by regulation, the Pediatric Research Equity Act does not apply to any drug for an indication for which orphan designation has been granted. However, if only one indication for a product has orphan designation, a pediatric assessment may still be required for any applications to market that same product for the non-orphan indication(s).

The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the Prescription Drug User Fee Act (“PDUFA”), guidelines that are currently in effect, the FDA has a goal of ten months from the date of “filing” of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a “filing” decision after it the application is submitted. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often significantly extended by FDA requests for additional information or clarification.

After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use and whether the product is being manufactured in accordance with cGMP to assure and preserve the product’s identity, strength, quality and purity. The FDA may refer applications for novel drug products or drug 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 and typically follows the advisory committee’s recommendations.

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 may inspect one or more clinical sites to assure compliance with GCP requirements. After the FDA evaluates the application, manufacturing process and manufacturing facilities, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data and/or (an) additional pivotal Phase 3 clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or

manufacturing. If a 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. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval.

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 or may condition the approval of the NDA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical trials. For example, the FDA may require Phase 4 testing, which involves clinical trials designed to further assess a drug safety and effectiveness, and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also determine that a risk evaluation and mitigation strategy (“REMS”) is necessary to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS; the FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools.

Orphan Drug Designation

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

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or inability to manufacture the product in sufficient quantities. The designation of such drug also entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug as defined by the FDA or if our product candidate is determined to be contained within the competitor’s product for the same indication or disease. If an orphan designated product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity. Orphan drug status in the European Union has similar but not identical benefits in that jurisdiction.

Rare Pediatric Disease Priority Review Voucher Program

In 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications. This provision is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a “rare pediatric disease” may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the U.S. within one year following the date of approval.

For the purposes of this program, a “rare pediatric disease” is a (a) serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents; and (b) rare disease or conditions within the meaning of the Orphan Drug Act. A sponsor may choose to request Rare Pediatric Disease Designation, but the designation process is entirely voluntary; requesting designation is not a prerequisite to requesting or receiving a priority review voucher. In addition, sponsors who choose not to submit a Rare Pediatric Disease Designation request may nonetheless receive a priority review voucher if they request such a voucher in their original marketing application and meet all of the eligibility criteria.

Expedited Development and Review Programs

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

Any product submitted to the FDA for approval, including a product with a fast track designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. A product is eligible for priority review if it has the potential to provide safe and effective therapy for a serious condition where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a serious condition compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review.

In addition, a product may be eligible for accelerated approval. Drug products intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. Fast track designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

A sponsor may seek FDA designation of a drug candidate as a “breakthrough therapy” if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes intensive FDA interaction and guidance. If a drug is designated as breakthrough therapy, the FDA will expedite the development and review of such drug. Breakthrough therapy designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance. The breakthrough therapy designation is a distinct status from both accelerated approval and priority review, which can also be granted to the same drug if relevant criteria are met. If a product is designated as breakthrough therapy, the FDA will work to expedite the development and review of such drug.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. In addition, this designation may not provide a material commercial advantage.

Post-Approval Requirements

Any drug 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, and complying with FDA promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use"), limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the internet. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses.

In addition, quality control and manufacturing procedures must continue to conform to applicable manufacturing requirements after approval to ensure the long term stability of the drug product. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs 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, among other things, recall or withdrawal of the product from the market. In addition, changes to the manufacturing process are strictly regulated, and depending on the significance of the change, may require prior FDA approval before being implemented. Other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

The FDA also may require post-marketing testing, known as Phase 4 testing, and surveillance to monitor the effects of an approved product. Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of the FDA approval of the use of our product candidates, some of our U.S. patents, if granted, 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 drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. 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 intend to apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA.

Market exclusivity provisions under the FDCA can also delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application (“ANDA”), or a 505(b)(2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. The FDCA alternatively provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances. Pediatric exclusivity is another type of non-patent 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 trial in accordance with an FDA-issued “Written Request” for such a trial.

Other U.S. Healthcare Laws and Compliance Requirements

Although we currently do not have any products on the market, we are and, upon approval and commercialization, will be subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. In the United States, such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security, price reporting, and health care provider sunshine laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor.

Additionally, the intent standard under the Anti-Kickback Statute and the criminal healthcare fraud statutes (discussed below) was amended by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the “Affordable Care Act”), to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the Affordable Care Act codified case law 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 federal False Claims Act (discussed below).

The federal False Claims Act, as well as the civil monetary penalty law, prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. As a result of a modification to the federal False Claims Act made by the Fraud Enforcement and Recovery Act of 2009, a claim includes “any request or demand” for money or property presented to the U.S. government. 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. Companies have also been prosecuted for causing false claims to be submitted because of the companies’ marketing of the product for unapproved, and thus non-covered, uses.

The Health Insurance Portability and Accountability Act (“HIPAA”) also created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, 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. Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Additionally, the federal Physician Payments Sunshine Act within the Affordable Care Act, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program (with certain exceptions) annually report information related to certain payments or other transfers of value made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, certain ownership and investment interests held by physicians and their immediate family members. Beginning in 2022, applicable manufacturers will also be required to report such information regarding payments and transfers of value provided during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified nurse anesthetists and certified nurse-midwives.

We may also be subject to data privacy and security regulations 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 (“HITECH”), and its implementing regulations, impose requirements 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, independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, 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 attorneys’ fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

We also are or will become subject to privacy laws in the jurisdictions in which we are established or in which we sell or market our products or run clinical trials. For example, in relation to clinical trials in Europe, we are subject to Regulation (EU) 2016/679, the General Data Protection Regulation and similar laws in European countries outside of the EU (collectively, the “GDPR”), in relation to our collection, control, processing and other use of personal data (i.e. data relating to an identifiable living individual). We process personal data in relation to participants in our clinical trials in the European Economic Area, including the health and medical information of these participants. The GDPR also provides that European Union Member States may introduce further conditions, including limitations which could limit our ability to collect, use and share personal data (including health and medical information), or could cause our compliance costs to increase, ultimately having an adverse impact on our business. The GDPR imposes onerous accountability obligations requiring data controllers and processors to

maintain a record of their data processing and implement policies as part of its mandated privacy governance framework. It also requires data controllers to be transparent and disclose to data subjects (in a concise, intelligible and easily accessible form) how their personal information is to be used, imposes limitations on retention of personal data; defines for the first time pseudonymized (i.e., key-coded) data; introduces mandatory data breach notification requirements; and sets higher standards for data controllers to demonstrate that they have obtained valid consent for certain data processing activities. We are also subject to European Union rules with respect to cross-border transfers of personal data out of the European Union and European Economic Area. We are subject to the supervision of local data protection authorities in those European Union jurisdictions where we are established or otherwise subject to the GDPR, and we maintain an office in Switzerland, which has similar privacy and data protection laws and regulations. Fines for certain breaches of the GDPR are significant: up to the greater of €20 million or 4% of total global annual turnover. In addition to the foregoing, a breach of the GDPR or other applicable privacy and data protection laws and regulations could result in regulatory investigations, reputational damage, orders to cease/change our use of data, enforcement notices, or potential civil claims including class action type litigation.

In addition, California recently enacted the California Consumer Privacy Act (“CCPA”), which requires covered companies to provide new disclosures to California residents and honor their requests to access, delete and opt-out of certain sharing of their personal data. The CCPA, which took effect on January 1, 2020, provides for civil penalties for violations and statutory damages for certain data breaches. The CCPA will expand substantially as a result of California voters approving a November 2020 ballot measure that adopted the California Privacy Rights Act of 2020, which will, among other things, create a new administrative agency to implement and enforce California’s privacy laws effective January 1, 2023. While certain clinical trial activities are exempt from the CCPA’s requirements, other personal information that we handle may be subject to the CCPA, which may increase our compliance costs, exposure to regulatory enforcement action and other liabilities.

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

If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including without limitation, significant civil, criminal and/or administrative penalties, damages, fines, disgorgement, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, imprisonment, private “qui tam” actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we or our collaborators obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we or our collaborators receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage, and establish adequate reimbursement levels for such drug products.

In the United States, third-party payors include federal and state healthcare programs, government authorities, private managed care providers, private health insurers and other organizations. Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical drug products and medical services, in addition to questioning their safety and efficacy. Such payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the FDA-approved drugs for a particular indication. We or our collaborators may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Nonetheless, our product candidates may not be considered medically necessary or cost-effective. Moreover, the process for determining whether a third-party payor will provide coverage for a drug product may be separate from the process for setting the price of a drug product or for establishing the reimbursement rate that such a payor will pay for the drug product. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. 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.

If we elect to participate in certain governmental programs, we may be required to participate in discount and rebate programs, which may result in prices for our future products that will likely be lower than the prices we might otherwise obtain. For example, drug manufacturers participating under the Medicaid Drug Rebate Program must pay rebates on prescription drugs to state Medicaid programs. Under the Veterans Health Care Act ("VHCA"), drug companies are required to offer certain drugs at a reduced price to a number of federal agencies, including the U.S. Department of Veterans Affairs and Department of Defense, the Public Health Service and certain private Public Health Service designated entities in order to participate in other federal funding programs, including Medicare and Medicaid. Recent legislative changes require that discounted prices be offered for certain U.S. Department of Defense purchases for its TRICARE program via a rebate system. Participation under the VHCA also requires submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, as well as the entry into government procurement contracts governed by the Federal Acquisition Regulations. If our products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply.

Different pricing and reimbursement schemes exist in other countries. In the European Union, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular drug candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on 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 product candidates for which we or our collaborators 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 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 or our collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products and services, implementing reductions in Medicare and other healthcare funding and applying new payment methodologies. For example, in March 2010, the Affordable Care Act was enacted, which affected existing government healthcare programs and resulted in the development of new programs.

Among the Affordable Care Act's provisions of importance to the pharmaceutical industry, in addition to those otherwise described above, are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively, and a cap on the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price ("AMP");
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturers' 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, including 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; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

There have been executive, judicial and Congressional challenges to certain aspects of the Affordable Care Act. For example, the Tax Act was enacted, which included a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas ruled that the individual mandate is a critical and inseparable feature of the Affordable Care Act, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the Affordable Care Act are invalid as well. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit ruled that that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. The U.S. Supreme Court is currently reviewing this case, but it is unknown when a decision will be reached. Although the Supreme Court has not yet ruled on the constitutionality of the Affordable Care Act, on January 28, 2021, the current administration issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the Affordable Care Act 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 Affordable Care Act. It is unclear how the Supreme Court ruling, other such litigation and the healthcare reform measures of the current administration will impact the Affordable Care Act and our business.

Other legislative changes have also been proposed and adopted in the United States since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030 unless additional Congressional action is taken. However, COVID-19 relief legislation suspended the 2% Medicare sequester from

May 1, 2020 through March 31, 2021. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There has been heightened governmental scrutiny recently over the manner in which pharmaceutical companies set prices for their marketed products, which has resulted in several Congressional inquiries and proposed federal legislation, as well as state efforts, designed to, among other things, bring more transparency to product pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products

At the federal level, the previous 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 previous 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, 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, the U.S. Department of Health and Human Services 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 current 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 current administration until March 22, 2021. On November 20, 2020, Centers for Medicare & Medicaid Services issued an interim final rule implementing the previous administration'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, effective January 1, 2021. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. It is unclear what additional reform measures, if any, will be taken by the current administration related to drug pricing reform on a federal level.

At the state level, individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs.

We anticipate that these new laws will result in additional downward pressure on coverage and the price that we receive for any approved product, and could seriously harm our business. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. In addition, it is possible that there will be further legislation or regulation that could harm our business, financial condition, and results of operations. Further, it is possible that additional governmental action will be taken in response to the COVID-19 pandemic.

The U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act of 1977 ("FCPA"), prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international

subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Europe / Rest of World Government Regulation

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. Whether or not we or our potential collaborators obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of an application for a clinical trial authorization (“CTA”), much like the IND prior to the commencement of human clinical trials. In the European Union, for example, a CTA must be submitted to each country’s national health authority and an application made to an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country’s requirements and a favorable ethics committee opinion has been issued, clinical trial development may proceed.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational drug or biological product under European Union regulatory systems, we must submit an MAA either under the so-called centralized or national authorization procedures.

Centralized procedure. The centralized procedure provides for the grant of a single marketing authorization by the European Commission following a favorable opinion by the EMA that is valid in all European Union member states, as well as Iceland, Liechtenstein and Norway. The centralized procedure is compulsory for medicines produced by specified biotechnological processes, products designated as orphan medicinal products, and products with a new active substance indicated for the treatment of specified diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases, other immune dysfunctions and viral diseases. The centralized procedure is optional for other products that represent a significant therapeutic, scientific or technical innovation, or whose authorization would be in the interest of public health or which contain a new active substance for indications other than those specified to be compulsory.

National authorization procedures. There are also two other possible routes to authorize medicinal products in several European Union countries, which are available for investigational medicinal products that fall outside the scope of the centralized procedure:

- *Decentralized procedure.* Using the decentralized procedure, an applicant may apply for simultaneous authorizations in more than one European Union Member State of medicinal products that have not yet been authorized in any European Union Member State and that do not fall within the mandatory scope of the centralized procedure.
- *Mutual recognition procedure.* In the mutual recognition procedure, a medicine is first authorized in one European Union Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other European Union countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

The EMA grants orphan drug designation to promote the development of products for the treatment, prevention or diagnosis of life-threatening or chronically debilitating conditions affecting not more than five in 10,000 people in the European Union. In addition, orphan drug designation can be granted if the drug is intended for a life threatening or chronically debilitating condition in the European Union and without incentives it is unlikely that sales of the drug in the European Union would be sufficient to justify the investment required to develop the drug. Orphan drug designation is only available if there is no other satisfactory method approved in the European

Union of diagnosing, preventing or treating the condition, or if such a method exists, the proposed orphan drug will be of significant benefit to patients. Orphan drug designation provides opportunities for free or reduced-fee protocol assistance, fee reductions for MAAs and other post-authorization activities and ten years of market exclusivity following drug approval, which can be extended to 12 years if trials are conducted in accordance with an agreed-upon pediatric investigational plan. The exclusivity period may be reduced to six years if the designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

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

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

Human Capital Management

As of December 31, 2020, we employed 68 employees, all of whom are full-time, consisting of clinical, research, operations, finance and business development personnel. Seventeen of our employees hold Ph.D. or M.D. degrees. Further, 61 of our employees are located in the United States, and seven are located in Switzerland. None of our employees is subject to a collective bargaining agreement. We consider our relationship with our employees to be good.

We expect to continue to add employees in 2021, with a focus on clinical, research and development and commercialization activities. We continually evaluate the business need and opportunity to expand our team and balance in-house expertise and capacity with outsourced expertise and capacity. Currently, we outsource substantial clinical trial work to clinical research organizations and drug manufacturing to contract manufacturers.

We maintain a safety culture grounded on the premise of eliminating workplace incidents, risks and hazards. In response to COVID-19, we have implemented and continue to enhance safety measures in all our facilities, including:

- Making work-from-home the default for all employees.
- Establishing clear and regular COVID-19 policies, safety protocols and updates to all employees.
- If employees are required to work from an office location:
 - implementing daily health attestations and capacity management;
 - providing additional personal protective equipment and cleaning supplies;
 - increasing cleaning and sanitization protocols across all locations; and
 - requiring face coverings to be worn in all locations.
- Prohibiting all work-related domestic and international non-essential travel for all employees.

We believe our success depends on our ability to attract, develop and retain key personnel. We invest in the growth and development of our employees through various training and development programs that build and strengthen employees' leadership and professional skills. We also have processes in place to conduct activities like performance management, succession and workforce planning in order to support our employees in their growth and development and ensure we provide learning opportunities.

To continually assess and improve our employee retention and engagement, we conduct an engagement survey on a regular basis, the results of which are discussed with our board of directors, at all-hands employee meetings and

in individual functions. We take actions to address areas of employment concern and follow up routinely to share with employees what we are doing.

We strive toward having a diverse team of employees and are committed to equality, inclusion and workplace diversity. To accomplish this, we have included questions in our engagement survey to measure employee perception of inclusive culture. In 2020, we established a Culture Team consisting of four employees across a representative cross-section of departments. Amongst other initiatives, our Culture Team engages in continual discussions across the various business functions to identify potential actions to address areas of improvement and is focused on building accountability across the organization to ensure we meet our diversity objectives.

Corporate Information

We were incorporated in Delaware in May 2018. Our principal executive offices are located at 950 Tower Lane, Suite 1050, Foster City, California 94404, and our telephone number is (650) 667-4085. Our corporate website address is www.mirumpharma.com. Information contained on or accessible through our website is not a part of this Annual Report, and the inclusion of our website address in this report is an inactive textual reference only. Our design logo, “Mirum,” and our other registered and common law trade names, trademarks and service marks are the property of Mirum Pharmaceuticals, Inc.

Emerging Growth Company

We are an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012 (“JOBS Act”). We may take advantage of certain exemptions from various public company reporting requirements, including not being required to have our internal control over financial reporting audited by our independent registered public accounting firm under Section 404 of the Sarbanes-Oxley Act of 2002 (“Sarbanes-Oxley Act”), reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and any golden parachute payments. We may take advantage of these exemptions until December 31, 2024 or until we are no longer an “emerging growth company,” whichever is earlier. We will cease to be an emerging growth company prior to the end of such period if certain earlier events occur, including if we become a “large accelerated filer” as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended (“Exchange Act”), our annual gross revenues exceed \$1.07 billion or we issue more than \$1.0 billion of non-convertible debt in any three-year period.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This provision allows an emerging growth company to delay the adoption of accounting standards that have different effective dates for public and private companies until those standards would otherwise apply to private companies. We have not elected to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not “emerging growth companies.”

We are also a “smaller reporting company” as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as our voting and non-voting common stock held by non-affiliates is less than \$250.0 million measured on the last business day of our second fiscal quarter, or our annual revenue is less than \$100.0 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is less than \$700.0 million measured on the last business day of our second fiscal quarter.

Item 1A. Risk Factors.

An investment in shares of our common stock involves a high degree of risk. You should carefully consider the following risk factors, as well as the other information in this Annual Report on Form 10-K, before deciding whether to purchase, hold or sell shares of our common stock. The occurrence of any of the following risks could harm our business, financial condition, results of operations and/or growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made in this Annual Report on Form 10-K and those we may make from time to time. You should consider all of the risk factors described when evaluating our business.

Risks Related to Our Business and Industry

We have a very limited operating history, and we have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.

We were incorporated in May 2018 and commenced operations in November 2018, and we have a very limited operating history upon which you can evaluate our business and prospects. Our operations to date have been primarily focused on acquiring and in-licensing our product candidates, maralixibat and volixibat, organizing and staffing our company, business planning, raising capital, advancing our product candidates through clinical development and preparing for commercialization of maralixibat. We have not yet demonstrated an ability to overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. We have not yet demonstrated an ability to obtain regulatory approval for, or to commercialize, a product candidate. Consequently, any predictions about our future performance may not be as accurate as they would be if we had a history of successfully developing and commercializing biopharmaceutical products.

Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effectiveness in the targeted indication or an acceptable safety profile, gain regulatory approval and become commercially viable. We have no products approved for commercial sale and have not generated any revenue to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we are not profitable and have incurred significant losses since our inception in May 2018. For the years ended December 31, 2020, December 31, 2019 and for the period from May 2, 2018 (inception) to December 31, 2018, we reported a net loss of \$103.3 million, \$52.6 million and \$17.3 million, respectively. As of December 31, 2020, we had an accumulated deficit of \$173.2 million.

We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our clinical development of, and seek regulatory approvals for, our product candidates. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. Because of the numerous risks and uncertainties associated with drug development, we are unable to accurately predict the timing or amount of increased expenses, or when, if at all, we will be able to achieve profitability.

Our business has been and could continue to be adversely affected by the COVID-19 pandemic in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of clinical trial sites or other business operations. The COVID-19 pandemic could adversely affect our operations, including our workforce, which is currently primarily working remotely and at our clinical trial sites, as well as the business or operations of our manufacturers, clinical research organizations (“CROs”) or other third parties with whom we conduct business.

Our business has been and could continue to be adversely affected by the global COVID-19 pandemic. In response to the COVID-19 pandemic, we have implemented work-from-home policies for all of our employees. The effects of the COVID-19 pandemic and our work-from-home policies may negatively impact productivity, disrupt our business and delay our clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of any restrictions and limitations on our ability to conduct our business in the ordinary course. These and similar, and perhaps more severe, disruptions in our operations could negatively impact our business, operating results and financial condition.

As a result of COVID-19, we may experience, or continue to experience, ongoing disruptions that could severely impact our business and clinical trials, including:

- delays or difficulties in enrolling and retaining patients in our ongoing and planned clinical trials;
- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials, including interruption in global shipping that may affect the transport of clinical trial materials;
- changes in local regulations as part of a response to the COVID-19 outbreak which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others, or interruption of clinical trial subject visits and study procedures, the occurrence of which could affect the integrity of clinical trial data;
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- risk that participants enrolled in our clinical trials will acquire COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events; and
- refusal of the FDA or other regulatory authorities to accept data from clinical trials in affected geographies.

These and other disruptions in our operations and the global economy could negatively impact our business, operating results and financial condition.

Our clinical trials have been, and may in the future be, affected by the COVID-19 pandemic. For example, the COVID-19 pandemic has impacted patient enrollment in our Phase 3 MARCH clinical trial. In particular, at times, some sites have paused enrollment to focus on, and direct resources to, COVID-19, while at other sites, patients are choosing not to enroll or continue participating in the clinical trial as a result of the pandemic. If patient enrollment is delayed for an extended period of time, our Phase 3 MARCH clinical trial could be further delayed or otherwise

adversely affected. Similarly, our ability to recruit and retain principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19, may be adversely impacted.

Our ongoing or planned clinical trials may also be impacted by interruptions or delays in the operations of the FDA and comparable foreign regulatory agencies. For example, the inability of the FDA to inspect foreign manufacturing sites due to COVID-19-related travel restrictions may interrupt or delay our NDA reviews. Any potential interruptions or delays could adversely affect the anticipated timelines of our NDA and MAA reviews.

We and our CROs have also made certain adjustments to the operation of our trials in an effort to ensure the monitoring and safety of patients and minimize risks to trial integrity during the pandemic in accordance with the guidance issued by the FDA on March 18, 2020 and subsequently updated, and may need to make further adjustments in the future. For example, in our ongoing clinical trials, we have adopted new protocols to allow for flexibility surrounding patient visits, including to have drug shipped to them and for patients to virtually check-in as opposed to attending standard hospital visits. Many of these adjustments are new and untested, may not be effective, and may have unforeseen effects on the progress and completion of this clinical trial and the findings from this clinical trial. In addition, we may encounter delays in shipping of our study drug. These events could delay our clinical trials, increase the cost of completing our clinical trials and negatively impact the integrity, reliability or robustness of the data from our clinical trials.

In addition, quarantines, shelter-in-place and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, related to COVID-19 or other infectious diseases could impact personnel at our CROs or third-party manufacturing facilities upon which we rely, or the availability or cost of materials, which could disrupt the supply chain for our product candidates. To the extent our suppliers and service providers are unable to comply with their obligations under our agreements with them or they are otherwise unable to deliver or are delayed in delivering goods and services to us due to the COVID-19 pandemic, our ability to continue meeting clinical supply demand for our product candidates or otherwise advancing development of our product candidates may become impaired.

The spread of COVID-19 and actions taken to reduce its spread may also materially affect us economically. While the potential economic impact brought by, and the duration of, the COVID-19 pandemic may be difficult to assess or predict, there could be a significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity and financial position. In addition, the trading prices for other biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic. As a result, we may face difficulties raising capital through sales of our common stock or such sales may be on unfavorable terms.

COVID-19 and actions taken to reduce its spread continue to evolve. The extent to which COVID-19 may impede the development and commercialization of our product candidates, reduce the productivity of our employees, disrupt our supply chains, delay our clinical trials, reduce our access to capital or limit our business development activities, will depend on future developments, which are highly uncertain and cannot be predicted with confidence.

In addition, to the extent the ongoing COVID-19 pandemic adversely affects our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties described in this “Risk Factors” section.

Our business is dependent on the success of our product candidates, each of which require significant clinical testing before we can seek regulatory approval and potentially launch commercial sales.

Our business and future success depends on our ability to obtain regulatory approval for, and then successfully commercialize, maralixibat and volixibat. We currently generate no revenues from sales of any of our product candidates, and we may never be able to develop a marketable product. Our product candidates will require clinical development, regulatory review and approval in multiple jurisdictions, substantial investment, access to sufficient manufacturing capacity and significant marketing efforts before we can generate any revenues from product sales. Further, we are not permitted to market or promote any of our product candidates before we receive regulatory

approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approvals.

Our clinical trials may not be successful and may not be completed on time or at all, and the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials. For example, in certain of our planned and ongoing clinical trials, the primary efficacy endpoint is a patient-reported outcome or a caregiver-reported outcome measuring the decrease in severity of pruritus. The FDA or comparable foreign regulatory authority may not accept such patient-reported outcomes or caregiver-reported outcomes as validated. If modifications are needed for our study design to support the submission of an application for marketing approval, incorporating such modifications may be costly and could lead to delays in obtaining approval from the FDA or comparable foreign regulatory authorities, which may significantly, adversely and materially affect our ability to successfully commercialize our product candidates. Further, even if we make changes to the study design to address these considerations, the FDA or comparable foreign regulatory authorities may not approve our product candidates.

Even if such regulatory authorities agree with the design and implementation of our clinical trials, such regulatory authorities may change their requirements in the future. In addition, even if the clinical trials are successfully completed, the FDA or foreign regulatory authorities may not interpret the results as we do, and more clinical trials could be required before we submit our product candidates for approval. For example, the FDA typically requires results from two well controlled Phase 3 clinical trials to support an NDA submission seeking approval to market a new drug. Based on interactions with the FDA, we believe that the results from a single Phase 3 clinical trial, if successful, would be sufficient to support an NDA submission seeking approval for maralixibat for the treatment of pruritus associated with PFIC2; however, the FDA may not agree to this approach. Even if we believe the results from our Phase 3 clinical trials are positive, the FDA may require us to conduct additional Phase 3 trials before we are able to submit one or more NDAs. Moreover, based on interactions with the FDA, we believe that clinical data of maralixibat in PFIC2 paired with adequate natural history data may be adequate to support an NDA filing for a general PFIC2 indication rather than the treatment of pruritus associated with PFIC; however, the FDA has not agreed to this approach but has indicated that efficacy data of the Phase 3 MARCH clinical trial, if positive, may be adequate to support an NDA submission for the treatment of pruritus associated with nt-PFIC2. If we are unable to obtain adequate natural history data or the FDA does not view such data as sufficient to support approval for a general PFIC indication, the NDA submission for maralixibat may be limited to the treatment of pruritus associated with nt-PFIC2. Further, we have conducted an initial analysis of our long-term treatment data in PFIC against a natural history control group in conjunction with the NAPPED Consortium and have shared these results with regulatory authorities. Based on feedback from regulatory authorities, we submitted an MAA for the treatment of PFIC2 to the EMA in the fourth quarter of 2020. However, regulatory authorities may not view such initial analysis as sufficient to support approval.

In May 2019, we had an end-of-Phase 2 meeting with the FDA to discuss the adequacy of the current data set of maralixibat to support an NDA submission for the treatment of pruritus associated with ALGS. At the request of the FDA, we prepared various analyses of the maralixibat data set, in particular the ICONIC clinical trial as the potential pivotal study, and requested an additional meeting with the FDA. In October 2019, the FDA requested that we convert the meeting to a pre-NDA meeting and discuss the components and timeline of an NDA submission. During this meeting, we and the FDA reached consensus on a timeline for initiating a rolling submission of an NDA in the third quarter of 2020 and the details of various routine datasets to generate for the submission. The rolling submission was initiated on August 31, 2020 and we completed the NDA submission in the first quarter of 2021. The NDA includes extensive clinical and preclinical data, as well as extensive information regarding pharmacology and chemistry, manufacturing and controls (“CMC”). The FDA may disagree with our interpretation of such data and information, which may require us to complete additional activities. As a result, FDA approval of maralixibat for cholestatic pruritus in patients with ALGS may be delayed and we may be required to expend significant additional resources seeking such approval. Moreover, although we are in the process of discussing our planned ALGS registrational program with the EMA, we have not reached agreement, and the EMA may not accept our currently proposed ALGS registrational program.

To the extent that the results of our clinical trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, approval for our product candidates may be significantly delayed

or prevented, or we may be required to expend significant additional resources, which may not be available to us, to conduct additional clinical trials in support of potential approval for our product candidates. Even if we are able to obtain approval for any product candidate, the approved label may be limited to a symptom of the target disease, such as pruritus, or subset of the patient population, such as patients with nt-PFIC2.

We have encountered and may continue to encounter delays and difficulties enrolling patients in our clinical trials, and as a result, our clinical development activities could be delayed or otherwise adversely affected.

Patient enrollment, a significant factor in the timing of clinical trials, is generally affected by many factors including, but not limited to, the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the clinical trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

The COVID-19 pandemic has impacted patient enrollment in our Phase 3 MARCH clinical trial. If patient enrollment is delayed for an extended period of time, our Phase 3 MARCH clinical trial could be further delayed or otherwise adversely affected.

Further, each indication for which we are evaluating maralixibat and volixibat is a rare cholestatic liver disease with limited patient populations from which to draw participants in clinical trials. We will be required to identify and enroll a sufficient number of patients with the disease under investigation for each of our ongoing and planned clinical trials of maralixibat and volixibat. Potential patients may not be adequately diagnosed or identified with the diseases which we are targeting or may not meet the entry criteria for our studies. For example, many patients with PFIC seek liver transplants early and as a result become ineligible for our treatment. In addition, we are conducting clinical trials in countries that have not yet had maralixibat or volixibat trials conducted and we have not yet worked with such foreign regulatory authorities. As a result, we could face patient recruitment issues in certain countries where such foreign regulatory authorities are not familiar with maralixibat or volixibat. Additionally, other pharmaceutical companies targeting these same cholestatic liver diseases are recruiting clinical trial patients from these patient populations, and have expanded access programs available, which may delay or make it more difficult to fully enroll our clinical trials. Our inability to enroll a sufficient number of patients for any of our current or future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. As a result, we may experience new or additional delays and difficulties in enrollment, which would result in the delay of completion of such trials beyond our expected timelines.

Our clinical trials may fail to adequately demonstrate the safety and efficacy of our product candidates, which could prevent or delay regulatory approval and commercialization.

Before obtaining regulatory approvals for the commercial sale of a product candidate, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that a product candidate is both safe and effective for use in each target indication. Clinical trials often fail to demonstrate safety and efficacy of the product candidate studied for the target indication. Most product candidates that commence clinical trials are never approved by regulatory authorities for commercialization. In the case of maralixibat and volixibat, we are seeking to develop treatments for rare cholestatic liver diseases for which there is limited clinical experience, and our planned clinical trials use novel end points and measurement methodologies, which add complexity to the conduct of and analysis of data from our clinical trials and may delay or prevent regulatory approval. Importantly, because the measure of pruritus relies on subjective patient feedback, it is inherently difficult to evaluate, and is subject to placebo effect. It can be influenced by factors outside of our control and can vary widely from day to day for a particular patient, and from patient to patient and site to site within a clinical trial. The placebo effect may also have a significant impact on pruritus trials.

Clinical drug development involves a lengthy and expensive process with uncertain outcomes, and results of earlier studies and trials may not be predictive of future trial results.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. For example, volixibat has been evaluated primarily for the treatment of non-alcoholic steatohepatitis and has not been evaluated in ICP, PSC or PBC, and our clinical development strategy is predicated on observations of apical sodium-dependent bile acid transporter (“ASBT”) inhibition in cholestatic settings. Similarly, maralixibat has not yet been evaluated in BA or in subjects under 12 months of age. As such, our hypothesis of efficacy in these diseases will be evaluated in these target patient populations and may not show the desired clinical results. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or safety profiles, notwithstanding promising results in earlier trials. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses. For example, in the Phase 2 INDIGO clinical trial evaluating maralixibat in PFIC1 and PFIC2 patients, the primary efficacy analysis of serum bile acids (“sBA”) change from baseline to week 13 did not reach statistical significance for the overall group; however, a 48-week analysis of the clinical trial demonstrated a profound treatment response in a subset of patients with nt-PFIC2. In addition, we do not have experience in conducting placebo-controlled studies for PFIC, and we expect to administer higher doses of maralixibat than we previously have administered in this setting. We may face significant setbacks as we conduct our placebo-controlled Phase 3 clinical trial in PFIC, which may delay or prevent regulatory approval of maralixibat. Further, as a result of the COVID-19 pandemic, if patients drop out of our clinical trials, miss scheduled doses or follow-up visits or otherwise fail to follow clinical trial protocols, or if our clinical trials are otherwise disrupted due to COVID-19 or actions taken to slow its spread, the integrity of data from our clinical trials may be compromised or not accepted by the FDA or other regulatory authorities, which would represent a significant setback for the applicable program.

In addition, in the third quarter of 2020, we initiated an expanded access program for maralixibat in ALGS. Additional safety data generated from the expanded access program could be different from, including less favorable than, the data generated and discussed with regulatory authorities to date, which may delay or prevent regulatory approval of maralixibat.

Our planned clinical trials may not be successful, and any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in other indications.

Any delays in the commencement or completion, or termination or suspension, of our clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.

Before we can initiate clinical trials for our product candidates, we must submit the results of preclinical studies to the FDA or comparable foreign regulatory authorities along with other information, including information about product candidate CMC and our proposed clinical trial protocol, as part of an IND application or similar regulatory filing. Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive, time consuming and uncertain as to outcome. In addition, we may rely in part on preclinical, clinical and quality data generated by CROs, and other third parties for regulatory submissions for our product candidates. While we have or will have agreements governing these third parties’ services, we have limited influence over their actual performance. If these third parties do not make data available to us, or, if applicable, do not make regulatory submissions in a timely manner, in each case pursuant to our agreements with them, our development programs may be significantly delayed, and we may need to conduct additional studies or collect additional data independently. In either case, our development costs would increase.

We do not know whether our planned clinical trials will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical trials or agreement to commence our clinical trials;
- the FDA or comparable foreign regulatory authorities' failure to accept our proposed manufacturing processes and suppliers and/or requirement to provide additional information regarding our manufacturing processes before providing marketing authorization;
- any failure or delay in reaching an agreement with CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- obtaining approval from one or more IRBs;
- IRBs refusing to approve, suspending or terminating the clinical trial at an investigational site, precluding enrollment of additional subjects, or withdrawing their approval of the clinical trial;
- changes to clinical trial protocol;
- selection of clinical end points that require prolonged periods of clinical observation or analysis of the resulting data;
- sites deviating from clinical trial protocol or dropping out of a clinical trial;
- manufacturing sufficient quantities of product candidate or obtaining sufficient quantities of combination therapies for use in clinical trials;
- subjects failing to enroll or remain in our trial at the rate we expect, or failing to return for post-treatment follow-up;
- subjects choosing an alternative treatment for the indication for which we are developing our product candidates, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trial;
- subjects experiencing severe or unexpected drug-related adverse effects;
- occurrence of serious adverse events ("SAEs") in clinical trials of the same class of agents conducted by other companies;
- a facility manufacturing our product candidates or any of their components being ordered by the FDA or comparable foreign regulatory authorities to temporarily or permanently shut down due to violations of cGMP, regulations or other applicable requirements, or infections or cross-contaminations of product candidates in the manufacturing process;
- any changes to our manufacturing process, suppliers or formulation that may be necessary or desired;
- third-party vendors not performing manufacturing and distribution services in a timely manner or to sufficient quality standards;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, GCP, or other regulatory requirements;
- third-party contractors not performing data collection or analysis in a timely or accurate manner;

- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications; or
- the impact of COVID-19 on our ongoing and planned clinical trials.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by a Data Safety Monitoring Board for such trial or by the FDA or comparable foreign regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

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

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. Moreover, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. Any delays to our clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize our product candidates and our competitors may be able to bring products to market before we do, and the commercial viability of our product candidates could be significantly reduced. Any of these occurrences may harm our business, financial condition and prospects significantly.

Our product candidates are subject to extensive regulation and compliance, which is costly and time consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates.

The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing and distribution of our product candidates are subject to extensive regulation by the FDA in the United States and by comparable foreign regulatory authorities in foreign markets. In the United States, we are not permitted to market our product candidates until we receive regulatory approval from the FDA. The process of obtaining regulatory approval is expensive, often takes many years following the commencement of clinical trials and can vary substantially based upon the type, complexity and novelty of the product candidates involved, as well as the target indications and patient population. Approval policies or regulations may change, and 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. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed.

Prior to obtaining approval to commercialize a product candidate in the United States or internationally, we must demonstrate with substantial evidence from adequate and well-controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory authorities, that such product candidates are safe and effective for their intended uses. Results from non-clinical studies and clinical trials can be interpreted in different ways. Even if we believe the non-clinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authorities, as the case may be, may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or may object to elements of our clinical development program.

Our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials or the validation of our caregiver and patient reported outcome instruments;
- serious and unexpected drug-related side effects may be experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- the FDA or comparable foreign regulatory authorities may not accept clinical data from trials which are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the United States;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for any of its proposed indications;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to satisfy the FDA or comparable foreign regulatory authorities to support the submission of an NDA or other comparable submissions in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;

- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Any of the above events could prevent us from achieving market approval of our product candidates and could substantially increase the costs of commercializing our product candidates. The demand for our product candidates could also be negatively impacted by any adverse effects of a competitor's product or treatment.

Of the large number of drugs in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects.

Even if we eventually complete clinical trials and receive approval of an NDA or foreign marketing application for our product candidates, the FDA or comparable foreign regulatory authority may grant approval contingent on the performance of costly additional clinical trials, including Phase 4 clinical trials, and/or the implementation of a risk evaluation and mitigation strategy ("REMS"), which may be required to ensure safe use of the drug after approval. The FDA or the comparable foreign regulatory authority also may approve a product candidate for a more limited indication or patient population than we originally requested, and the FDA or comparable foreign regulatory authority may not approve the labeling that we believe is necessary or desirable for the successful commercialization of a product. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects.

If the market opportunities for our product candidates are smaller than we believe they are, our future revenue may be adversely affected, and our business may suffer.

If the size of the market opportunities in each of our target indications is smaller than we anticipate, we may not be able to achieve profitability and growth. We focus our clinical development of maralixibat on treatments for rare pediatric cholestatic liver diseases with relatively small patient populations. Given the small number of patients who have the diseases that we are targeting with maralixibat, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare pediatric cholestatic liver diseases. We also plan to focus our clinical development of volixibat as a treatment for ICP, PSC and PBC, diseases with relatively small patient populations. In addition, our estimates of the patient populations for our target indications have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations, and market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. For example, while we are evaluating maralixibat in patients with different types of PFIC in our Phase 3 MARCH clinical trial, in prior studies of maralixibat, the Phase 2 INDIGO clinical trial in particular, all of the multi-parameter responders were in the nt-PFIC2 subpopulation. Further, the primary endpoint in our Phase 3 MARCH clinical trial is designed to evaluate maralixibat's effect on pruritus associated with nt-PFIC2. As such, even if our Phase 3 MARCH clinical trial shows positive results in other PFIC subgroups, the design of our clinical trial may limit the ability of our NDA to be approved beyond the nt-PFIC2 population, if at all. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for each of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share. Lastly, the potentially addressable patient population for PFIC and ALGS may even be further reduced as gene therapy products become more widely accepted and approved.

Obtaining and maintaining regulatory approval for a product candidate in one jurisdiction does not mean that we will be successful in obtaining regulatory approval for that product candidate in other jurisdictions.

Obtaining and maintaining regulatory approval for a product candidate in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, while a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA grants marketing approval for a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our product candidates is also subject to approval.

We have submitted an MAA to the EMA for approval of maralixibat for the treatment of PFIC2 in the European Union. As with the FDA, obtaining approval of an MAA from the EMA is a similarly lengthy and expensive process and the EMA has its own procedures for approval for product candidates. Regulatory authorities in jurisdictions outside of the United States and the European Union also have requirements for approval for product candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our product candidates in certain countries. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of any of our product candidates will be harmed, which would adversely affect our business, prospects, financial condition and results of operations.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval or result in significant negative consequences following marketing approval, if any.

As is the case with biopharmaceuticals generally, it is likely that there may be side effects and adverse events associated with our product candidates' use. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. For example, we have observed increases in alanine aminotransferase ("ALT"), levels in certain patients being treated with maralixibat with ALGS. In addition, we intend to use higher doses of maralixibat and volixibat in future clinical trials. The use of higher doses could result in more frequent or more severe side effects. Furthermore, only patients 12 months of age and older have been treated with maralixibat, and the safety profile in patients under 12 months of age is unknown and may be different than that observed in previous clinical trials. Results of our trials could reveal a high and unacceptable severity and frequency of these or other side effects.

In clinical trials of maralixibat, the most commonly reported adverse events ("AEs") and SAEs have been those of gastrointestinal ("GI"), disorders such as diarrhea, abdominal pain and vomiting, and were mostly mild to moderate in severity and transient in nature. Reported treatment-related SAEs have consisted of abdominal pain, upper abdominal pain, diarrhea, cholangitis, increase in blood bilirubin, increase in international normalized ratio, pancreatitis, elevated ALT, autoimmune hepatitis, hematochezia, pure red cell aplasia, myelodysplastic syndrome and anemia. The frequency of observed AEs and SAEs has not increased over time. In Phase 1 clinical trials of volixibat, the most common AEs reported were mild to moderate GI events observed in the volixibat groups. The only treatment-related SAE reported was one event of elevated ALT.

In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval for our product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients

to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

In addition, in the third quarter of 2020, we initiated an expanded access program for maralixibat in ALGS. Patients who receive access to unapproved drugs through compassionate use or expanded access programs have life-threatening illnesses and generally have exhausted all other available therapies. The risk for SAEs, including those which may be unrelated to maralixibat, in this patient population is high and could have a negative impact on the safety profile of maralixibat, which could cause significant delays or impair our ability to obtain regulatory approval for maralixibat.

Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such product candidates, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

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

If we receive regulatory approval for a product candidate, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with any product.

Any regulatory approvals that we receive may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including post-market studies or clinical trials, and surveillance to monitor safety and effectiveness. The FDA may also require a REMS in order to approve a product candidate, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves a product candidate, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for the approved product will be subject to extensive and ongoing regulatory requirements. For example, the FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. The FDA also requires submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP requirements and GCP for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with a product candidate, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;

- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;
- product seizure or detention, or refusal to permit the import or export of a product; and
- injunctions or the imposition of civil or criminal penalties.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval for our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

We may pursue approval in the United States or Europe using accelerated approval or conditional approval pathways, which typically require commitments to complete additional clinical trials. The additional clinical trials may not confirm the treatment effect, which may result in the loss of marketing authorization under accelerated approval or conditional approval.

Disruptions at the FDA, EMA and other government agencies caused by funding shortages or global health concerns could negatively impact our business.

The ability of the FDA, EMA and other government agencies to review and approve proposed clinical trials or new product candidates can be affected by a variety of factors, including, but not limited to, government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, statutory, regulatory, and policy changes, and other events that may otherwise affect these regulatory agencies' ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA, EMA and other government agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the global COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most foreign inspections of manufacturing facilities and products through April 2020, and subsequently, on March 18, 2020, the FDA announced its intention to temporarily postpone routine surveillance inspections of domestic manufacturing facilities. On July 10, 2020, the FDA restarted routine pre-announced surveillance inspections of domestic manufacturing facilities on a risk-based basis. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Even if we obtain regulatory approval for our product candidates, our product candidates may not gain market acceptance among physicians, patients, tertiary care centers, transplant centers and others in the medical community.

If any one of our product candidates is approved for commercialization, its acceptance will depend on a number of factors, including:

- the clinical indications for which the product candidate is approved;
- physicians, major operators of tertiary care centers and transplant centers and patients considering the product as a safe and effective treatment;
- the potential and perceived advantages of the product over alternative treatments;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA or other regulatory authorities, including, in particular, whether the approved label is limited to the treatment of symptoms, such as pruritus, as compared to the treatment of the underlying disease;
- limitations or warnings contained in the labeling approved by the FDA or other regulatory authorities;
- the timing of market introduction of the product as well as competitive products;
- the cost of treatment in relation to alternative treatments;
- the availability of coverage and adequate reimbursement by third-party payors and government authorities;
- the willingness of patients to pay out-of-pocket in the absence of coverage and adequate reimbursement by third-party payors and government authorities;
- relative convenience and ease of administration, including as compared to alternative treatments and competitive therapies; and
- the effectiveness of our sales and marketing efforts.

If any of our product candidates are approved but fail to achieve market acceptance among physicians, patients or others in the medical community, we will not be able to generate significant revenues, which would have a material adverse effect on our business, prospects, financial condition and results of operations. In addition, even if any of our product candidates gain acceptance, the markets for the treatment of patients with our target indications for maralixibat may not be as significant as we estimate.

If our product candidates are approved for marketing, and we are found to have improperly promoted off-label uses, or if physicians prescribe our products or use our products off-label based on our product communications, we may become subject to prohibitions on the sale or marketing of our products, significant fines, penalties, sanctions, or product liability claims, and our image and reputation within the industry and marketplace could be harmed.

The FDA and comparable foreign authorities strictly regulate the marketing and promotional claims that are made about pharmaceutical products, such as our product candidates, if approved. In particular, a product may not be promoted for uses or indications that are not approved by the FDA or comparable foreign authorities as reflected in the product's approved labeling. If we receive marketing approval for maralixibat, physicians could prescribe maralixibat 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 receive warning letters from the FDA and comparable foreign authorities and become subject to significant liability, which would materially harm our business. Further, if such off-label promotion results in the submission of a reimbursement claim to a governmental healthcare program, we could be found liable under the U.S. False Claims Act. The federal government has levied significant civil and criminal penalties against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion and to undertake corrective remedies. If we become the target of such an investigation or prosecution based on our marketing and promotional practices, we could face similar sanctions, which would materially harm our business. In addition, management's attention could be diverted from our business operations, significant legal expenses could be incurred, and our reputation could be damaged. The FDA has also required that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed in order to resolve FDA enforcement actions. In cases where off-label promotion has resulted in violations of other statutes, the U.S. Department of Justice ("DOJ") has required companies to enter into deferred prosecution agreements or corporate integrity agreements. If we are deemed by the FDA or the DOJ to have engaged in the promotion of our products for off-label use, we could be subject to prohibitions or other restrictions on the sale or marketing of our products and other operations or significant fines and penalties, and the imposition of these sanctions could also affect our reputation and position within the industry.

Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, which could make it difficult for us to sell our product candidates profitably.

Successful sales of our product candidates, if approved, depend on the availability of coverage and adequate reimbursement from third-party payors. Patients who are prescribed medicine for the treatment of their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Coverage and adequate reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance, and we may not obtain such coverage or adequate reimbursement.

Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will cover and the amount of reimbursement they will provide. Reimbursement by a third-party payor may depend upon a number of factors, including, but not limited to, the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data for the use of our products. We may not be able to provide data sufficient to obtain coverage and adequate reimbursement. Assuming we obtain coverage for a given product, the resulting reimbursement

payment rates might not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use our product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates. Additionally, the reimbursement rates and coverage amounts may be affected by the approved label for our product candidates, including, in particular, whether the approved label is limited to the treatment of symptoms, such as pruritus, as compared to the treatment of the underlying disease. If coverage and reimbursement of our future products are unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

In addition, the market for our products will depend significantly on access to third-party payors' drug formularies or lists of medications for which third-party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access through formulary controls or otherwise to a branded drug when a less costly generic equivalent or other alternative is available.

In the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicare determinations. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

We intend to seek approval to market our product candidates in both the United States and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for a product candidate, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly those in the European Union, the pricing of prescription pharmaceuticals and biologics is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval for a drug candidate. In addition, market acceptance and sales of a product will depend significantly on the availability of coverage and adequate reimbursement from third-party payors for a product and may be affected by existing and future health care reform measures.

Recently enacted legislation, future legislation and healthcare reform measures may increase the difficulty and cost for us to obtain marketing approval for and commercialize our product candidates and may affect the prices we may set.

In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system, including cost-containment measures that may reduce or limit coverage and reimbursement for newly approved drugs and affect our ability to profitably sell any product candidates for which we obtain marketing approval. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare.

For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively "Affordable Care Act"), was enacted in the United States. Among the provisions of the Affordable Care Act of importance to our potential product candidates, the Affordable Care Act: established an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents; expanded eligibility criteria for Medicaid programs; increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program; creates a new Medicare Part D coverage gap discount program; established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare & Medicaid Innovation at the Centers for Medicare & Medicaid Services ("CMS") to test innovative payment and service delivery models to lower Medicare and Medicaid spending. At this time, we are unsure of the full impact that Affordable Care Act will have on our business. There have been

executive, judicial and Congressional challenges to certain aspects of the Affordable Care Act. For example, U.S. federal tax legislation enacted in 2017, informally titled The Tax Cuts and Jobs Act (“Tax Act”), included a provision which repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate.” On December 14, 2018, a Texas U.S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the “individual mandate” was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit ruled that that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. The U.S. Supreme Court is currently reviewing this case, but it is unknown when a decision will be reached. Although the Supreme Court has not yet ruled on the constitutionality of the Affordable Care Act, on January 28, 2021, the current administration issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the Affordable Care Act 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 Affordable Care Act. It is unclear how the Supreme Court ruling, other such litigation and the health care reform measures of the current administration will impact the Affordable Care Act and our business.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, included reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, including the Bipartisan Budget Act of 2018, will remain in effect through 2030 unless additional Congressional action is taken. However, COVID-19 relief legislation, suspended the 2% Medicare sequester from May 1, 2020 through March 31, 2021. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products.

At the federal level, the previous 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 previous 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, 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, the U.S. Department of Health and Human Services 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 current 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 current administration until March 22, 2021. On November 20, 2020, CMS issued an interim final rule implementing the previous administration’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, effective January 1, 2021. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. It is unclear what additional reform measures, if any, will be taken by the current administration related to drug pricing reform on a federal level.

At the state level, individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates, if approved, or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

We expect that the Affordable Care Act, these new laws and other healthcare reform measures that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from third-party payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates, if approved. In addition, it is possible that additional governmental action will be taken in response to the COVID-19 pandemic.

We currently have a limited marketing and sales organization and as a company, we have never commercialized a product before. If we are unable to adequately establish marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, we may not be able to generate viable product revenues. Even if we adequately establish such capabilities, market acceptance or reimbursement of our products may be lower than expected.

We currently do not have a full-scale commercial organization for the marketing, sales and distribution of pharmaceutical products. To commercialize our product candidates we must build our marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. We expect that the majority of PFIC and ALGS patients will be treated at tertiary care centers and transplant centers and therefore can be addressed with a targeted sales force. We intend to build our own commercial infrastructure in North America and in major European markets to target these centers, but will evaluate opportunities to partner with pharmaceutical companies that have established sales and marketing capabilities to commercialize our product candidates, if approved, outside of these geographies.

The establishment and development of our own sales force or the establishment of a contract sales force to market our product candidates will be expensive and time-consuming and could delay any commercial launch. Moreover, we may not be able to successfully or adequately develop this capability. We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates. To the extent we rely on third parties to commercialize our product candidates, if approved, we may have little or no control over the marketing and sales efforts of such third parties and our revenues from product sales may be lower than if we had commercialized our product candidates ourselves. In the event we are unable to develop our own marketing and sales force or collaborate with a third-party marketing and sales organization, we would not be able to commercialize our product candidates.

A variety of risks associated with marketing our product candidates internationally could materially adversely affect our business.

We plan to seek regulatory approval for our product candidates internationally and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including:

- differing regulatory requirements in foreign countries, including differing reimbursement, pricing and insurance regimes;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market (with low or lower prices) rather than buying them locally;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling internationally;
- 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;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the FCPA or comparable foreign regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities internationally; and
- business interruptions resulting from geo-political actions, including war and terrorism.

In addition, some countries, such as Brazil, require that clinical trial participants receive the product at no cost even after the clinical trial has ended. We would not be able to recover any profit for these patients and depending on the number of patients, duration of the treatment and numerous other factors, such regulations could harm our business, prospects, financial condition and results of operations significantly. These and other risks associated with our international operations may materially adversely affect our ability to attain or maintain profitable operations.

If we fail to develop and commercialize additional product candidates, we may be unable to grow our business.

Although we currently have no specific plans to do so, we may seek to develop and commercialize product candidates in addition to maralixibat and volixibat. If we decide to pursue the development and commercialization of any additional product candidates, we may be required to invest significant resources to acquire or in-license the rights to such product candidates or to conduct drug discovery activities. We do not currently have the necessary drug discovery personnel or expertise adequate to discover and develop an additional product candidate on our own. Any other product candidates will require additional, time-consuming development efforts, and significant financial resources, prior to commercial sale, including preclinical studies, extensive clinical trials and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent

in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and/or effective for approval by regulatory authorities. In addition, we may not be able to acquire, discover or develop any additional product candidates, and any additional product candidates we may develop may not be approved, manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective than other commercially available alternatives. Research programs to identify new product candidates require substantial technical, financial and human resources whether or not we ultimately identify any candidates. If we are unable to develop or commercialize any other product candidates, our business and prospects will suffer.

If we fail to develop our current and any future product candidates for additional indications, our commercial opportunity will be limited.

One of our strategies is to pursue clinical development of maralixibat in additional cholestatic disease conditions such as BA, benign recurrent intrahepatic cholestasis and drug-induced cholestasis. In addition, we are developing volixibat for the treatment of cholestatic liver diseases, including ICP, PSC and PBC.

The pediatric cholestatic liver diseases we are targeting are all rare diseases and, as a result, the market size for the treatment of patients with ALGS, PFIC and BA is limited. Due to these factors, our ability to grow revenues may be dependent on our ability to successfully develop and commercialize maralixibat for the treatment of additional indications. Developing, obtaining regulatory approval and commercializing maralixibat for additional indications will require substantial additional funding and is prone to the risks of failure inherent in drug development. We may not be able to successfully advance any of these indications through the development process. Even if we receive regulatory approval to market maralixibat for the treatment of any of these additional indications, any such additional indications may not be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives. If we are unable to successfully develop and commercialize maralixibat for these additional indications, our commercial opportunity will be limited.

We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.

The biopharmaceutical industry is characterized by intense competition and rapid innovation. Although we believe that we hold a leading position in our focus on rare pediatric cholestatic liver diseases, our competitors may be able to develop other compounds or drugs that are able to achieve similar or better results. Our potential competitors include major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies and universities and other research institutions. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations and well-established sales forces. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing, on an exclusive basis, drug products that are more effective or less costly than our product candidates. We believe the key competitive factors that will affect the development and commercial success of our product candidates are efficacy, safety and tolerability profile, reliability, convenience of dosing, price and reimbursement.

Outside of surgery, there are no approved therapies for the treatment of ALGS or PFIC in the United States. UDCA, which is approved for the treatment of PBC, is sometimes used to treat patients with other cholestatic liver diseases. Cholestyramine and other bile salt resins, rifampin, and naltrexone are sometimes used to treat patients suffering from pruritus, and a number of drugs, including UDCA, rifampin and naltrexone are used off-label to treat patients suffering from cholestatic liver disease. In addition, there are product candidates in development for some of these indications.

We are aware of two other companies pursuing clinical development of therapies that reduce sBA levels via the ASBT pathway. GlaxoSmithKline plc and Albireo have ASBTis in clinical development for cholestatic liver diseases. We are aware that Albireo has announced topline results from a Phase 3 trial for PFIC1 and PFIC2 patients for odevixibat, and has an extension study and an expanded access program enrolling PFIC patients. Albireo's NDA for odevixibat for the treatment of pruritus in patients with PFIC has been accepted by the FDA. Additionally, we are aware that Albireo has submitted an MAA for odevixibat. Albireo has also announced the initiation of studies of odevixibat in BA and ALGS and plans to pursue other cholestatic liver diseases. We are aware that GlaxoSmithKline plc has completed a Phase 2 trial of its ASBTi in PBC patients and has announced its intention to conduct a Phase 3 trial in PBC. We are also aware that Intercept Pharmaceuticals, Inc. is exploring BA as an indication for obeticholic acid. Further, we may compete with companies that are developing gene therapy for the treatment of PFIC. In adult settings of cholestasis, similar to pediatric settings, cholestyramine, UDCA, rifampin and naltrexone are commonly used agents. We are not aware of FDA approved therapeutics for the treatment of ICP or PSC. We are aware of several agents in clinical development for the treatment of PSC, including Cymabay's seladelpar, DURECT Corporation's DUR928, Gilead Sciences Inc.'s GS-9674, HighTide Biopharmaceutical Inc.'s HTD1801, Immunic Therapeutics' IMU-838, Intercept's Ocaliva, or obeticholic acid, NGM Biopharmaceuticals Inc.'s NGM282 and Pliant Therapeutics' PLN-74809. Intercept Pharmaceuticals, Inc.'s Ocaliva is approved as a second-line treatment for PBC. We are aware of several agents in clinical development for the treatment of PBC including Cymabay's seladelpar, Genfit's elafibranor and NGM Biopharmaceuticals, Inc.'s NGM282. Furthermore, if approved, one of our own product candidates may be used off-label in the market for another of our product candidates, adversely affecting the sales of that product candidate.

Even though we have obtained orphan drug designation for maralixibat in PFIC, ALGS and BA, we may not be able to obtain or maintain the benefits associated with orphan drug status, including market exclusivity.

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States, or a patient population of greater than 200,000 individuals in the United States, but for which there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the European Union, the EMA Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. In September 2013, the FDA granted orphan drug status to maralixibat for the treatment of patients with PFIC and ALGS in the United States. In October 2020, the FDA granted orphan drug status to maralixibat for the treatment of BA. We also received orphan drug status for maralixibat for PFIC, ALGS and BA in the European Union. Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug may be entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same drug for that time period. Another drug may receive marketing approval prior to our product candidates. The applicable period is seven years in the United States and ten years in the European Union, which may be extended by six months and two years, respectively, in the case of product candidates that have complied with the respective regulatory agency's agreed upon pediatric investigation plan. The exclusivity period in the European Union can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. In addition, even after a drug is granted orphan exclusivity and approved, the FDA can subsequently approve another drug for the same condition before the expiration of the seven-year exclusivity period if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In the European Union, the EMA may deny marketing approval for a product candidate if it determines such product candidate is structurally similar to an approved product for the same indication. For example, if a competing product is approved for ALGS or PFIC before maralixibat and is determined to be structurally similar by the EMA, maralixibat may be denied marketing authorization by EMA for that indication. In addition, if an orphan designated product receives marketing approval for an indication broader than or different from what is designated, such product may not be entitled to orphan exclusivity. Even though the FDA has granted orphan drug designation to maralixibat for the treatment of PFIC, ALGS and BA, if we receive approval for maralixibat for a modified or different indication, our current orphan designations may not provide us with exclusivity.

Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review or approval process. Also, regulatory approval for any product candidate may be withdrawn, and other product candidates may obtain approval before us and receive orphan drug exclusivity, which could block us from entering the market.

Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the candidate from competition because different drugs can be approved for the same condition before the expiration of the orphan drug exclusivity period.

Although we have received a breakthrough therapy designation for maralixibat, this may not lead to a faster development, regulatory review or approval process, and it does not increase the likelihood that maralixibat will receive marketing approval in the United States.

We have received a breakthrough therapy designation for maralixibat for the treatment of PFIC2 and for the treatment of pruritus associated with ALGS in patients one year of age and older. A breakthrough therapy is defined as a therapy that is intended, alone or in combination with one or more other therapies, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For therapies that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Therapies designated as breakthrough therapies by the FDA may also be eligible for priority review and accelerated approval. The breakthrough therapy designation for maralixibat may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, the FDA may later decide that maralixibat no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Although the FDA has granted Rare Pediatric Disease Designation for maralixibat for ALGS and PFIC, an NDA for maralixibat, if approved, may not meet the eligibility criteria for a priority review voucher.

Rare Pediatric Disease Designation has been granted for maralixibat for ALGS and PFIC. In 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications. This provision is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a “rare pediatric disease” may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the U.S. within one year following the date of approval.

For the purposes of this program, a “rare pediatric disease” is a (a) serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents; and (b) rare disease or conditions within the meaning of the Orphan Drug Act. Congress has only authorized the Rare Pediatric Disease Priority Review Voucher program until September 30, 2024. However, if a drug candidate receives Rare Pediatric Disease Designation before September 30, 2024, it is eligible to receive a voucher if it is approved before September 30, 2026.

However, maralixibat for ALGS or PFIC may not be approved by that date, or at all, and, therefore, we may not be in a position to obtain a priority review voucher prior to expiration of the program, unless Congress further reauthorizes the program. Additionally, designation of a drug for a rare pediatric disease does not guarantee that an NDA will meet the eligibility criteria for a rare pediatric disease priority review voucher at the time the application

is approved. Finally, a Rare Pediatric Disease Designation does not lead to faster development or regulatory review of the product, or increase the likelihood that it will receive marketing approval. We may or may not realize any benefit from receiving a voucher.

We may form or seek strategic alliances or enter into additional licensing arrangements in the future, and we may not realize the benefits of such alliances or licensing arrangements.

We may form or seek strategic alliances, create joint ventures or collaborations or enter into additional licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to maralixibat, volixibat and any future product candidates that we may develop. We intend to establish commercial partnerships outside of North America and in major European markets. Any of these relationships may require us to incur non-recurring and other charges, increase our near-and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for volixibat because it may be deemed to be at too early of a stage of development for collaborative effort, and third parties may not view volixibat as having the requisite potential to demonstrate safety and efficacy. If we license products or businesses, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture. Following a strategic transaction or license, we may not achieve the revenues or specific net income that justifies such transaction. Any delays in entering into new strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates in certain geographies for certain indications, which would harm our business prospects, financial condition and results of operations.

Our failure to successfully in-license, acquire, develop and market additional product candidates or approved products would impair our ability to grow our business.

Although a substantial amount of our efforts are focused on the clinical development, potential regulatory approval and commercialization of our product candidates, a key element of our long-term strategy is to in-license, acquire, develop, market and commercialize a portfolio of products to treat patients with liver disease. Because we do not have the necessary internal research and development capabilities, unless we build such capabilities internally, we will be dependent upon pharmaceutical companies, academic scientists and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify and select promising biopharmaceutical product candidates and products, negotiate licensing or acquisition agreements with their current owners and finance these arrangements. The process of proposing, negotiating and implementing a license or acquisition of a product candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing, sales and other resources, may compete with us for the license or acquisition of product candidates and approved products. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. We may not be able to acquire the rights to additional product candidates on terms that we find acceptable, or at all. Further, any product candidate that we acquire may require additional development efforts prior to commercial sale, including preclinical or clinical testing and approval by the FDA, the EMA and other similar regulatory authorities. All product candidates are prone to risks of failure during biopharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, any approved products that we acquire may not be manufactured or sold profitably or achieve market acceptance.

We are highly dependent on our key personnel, and if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, scientific and medical personnel. The loss of the services of any of our executive

officers or other key employees and our inability to find suitable replacements could potentially harm our business, prospects, financial condition or results of operations.

We conduct our operations at our facility in Foster City, California. This region serves as the headquarters to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel in our market is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided stock options that vest over time. The value to employees of stock options that vest over time may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. Although we have offer letters with our key employees, these offer letters provide for at-will employment, which means that any of our employees could leave our employment at any time, with or without notice. We do not maintain “key man” insurance policies on the lives of these individuals or the lives of any of our other employees. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level, and senior managers as well as junior, mid-level, and senior scientific and medical personnel.

Many of the other biotechnology and pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They may also provide more diverse opportunities and better chances for career advancement. Some of these characteristics are more appealing to high quality candidates than what we can offer. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can discover, develop and commercialize product candidates will be limited.

We will need to grow the size of our organization, and we may experience difficulties in managing this growth.

As of December 31, 2020, we had 68 full and part-time employees. As our development and commercialization plans and strategies develop, we expect to need additional development, managerial, operational, financial, sales, marketing and other personnel. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and regulatory review process for maralixibat and volixibat, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities. To date, we have used the services of outside vendors to perform tasks including clinical trial management, statistics and analysis, regulatory affairs, formulation development and other drug development functions. Our growth strategy may also entail expanding our group of contractors or consultants to implement these tasks going forward. Because we rely on numerous consultants, effectively outsourcing many key functions of our business, we will need to be able to effectively manage these consultants to ensure that they successfully carry out their contractual obligations and meet expected deadlines. However, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for our product candidates or otherwise advance our business. We may not be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, or at all. If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks

necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our research, development and commercialization goals.

Business disruptions could seriously harm our future revenues and financial condition and increase our costs and expenses.

Our operations, and those of our CROs and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or manmade disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce maralixibat and volixibat. Our ability to obtain clinical supplies of maralixibat and volixibat could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption. Our corporate headquarters is located in California near major earthquake faults and fire zones. The ultimate impact on us, our significant suppliers and our general infrastructure of being located near major earthquake faults and fire zones and being consolidated in certain geographical areas is unknown, but our operations and financial condition could suffer in the event of a major earthquake, fire or other natural disaster.

Our employees, independent contractors, principal investigators, CROs, consultants, strategic partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in fraudulent or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: (1) the laws of the FDA and other similar foreign regulatory bodies, including those laws that require the reporting of true, complete and accurate information to the FDA and other similar foreign regulatory bodies; (2) manufacturing standards; (3) healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws or (4) laws that require the true, complete and accurate reporting of our financial information or data. These laws may impact, among other things, our current activities with principal investigators and research subjects, as well as proposed and future sales, marketing and education programs. In particular, the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. If we obtain regulatory approval for any of our product candidates and begin commercializing those products in the United States and in the European Union, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, disgorgement, monetary fines, imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

Our relationships with customers, physicians and third-party payors may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, transparency laws, health information privacy and security laws and other healthcare laws and regulations. If we or our employees, independent contractors, consultants, commercial partners or vendors violate these laws, we could face substantial penalties.

These laws may impact, among other things, our clinical research program, as well as our proposed and future sales, marketing and education programs. In particular, the promotion, sales and marketing of healthcare items and services is subject to extensive laws and regulations designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive and other business arrangements. We may also be subject to federal, state and foreign laws governing the privacy and security of identifiable patient information. The U.S. healthcare laws and regulations that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, any person or entity from knowingly and willfully, offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, the purchasing, leasing, ordering or arranging for the purchase, lease, or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term “remuneration” has been broadly interpreted to include anything of value. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that may be alleged to be intended to induce prescribing, purchases or recommendations, include any payments of more than fair market value, and may be subject to scrutiny if they do not qualify for an exception or safe harbor. In addition, a person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act and the civil monetary penalties statute;
- federal civil and criminal false claims laws, including the federal civil False Claims Act, and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other federal government programs that are false or fraudulent or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government, including federal healthcare programs;
- Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), which created new federal civil and criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by any trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statements in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health (“HITECH”) Act, and their respective implementing regulations, which impose requirements on certain healthcare providers, health plans, and healthcare clearinghouses, known as covered entities and their respective business associates that perform services for them as well as their covered subcontractors that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information; and
- the federal Physician Payments Sunshine Act, which requires 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 to CMS information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Beginning in 2022, applicable manufacturers will also be required to report information regarding payments and other transfers of value provided during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives during the previous year.

We may also be subject to state and foreign equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope. For example, we may be subject to the following: state anti-kickback and false claims laws that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers, or that apply regardless of payor; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures, or drug pricing; state and local laws requiring the registration of pharmaceutical sales representatives; and state and foreign laws, such as the European Union's General Data Protection Regulation ("GDPR") governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Additionally, we may be subject to federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities, or our arrangements with physicians, could be subject to challenge under one or more of such laws. If we or our employees, independent contractors, consultants, commercial partners and vendors violate these laws, we may be subject to investigations, enforcement actions and/or significant penalties. We have adopted a code of conduct and healthcare compliance policies, but it is not always possible to identify and deter employee misconduct or business noncompliance, and the precautions we take to detect and prevent inappropriate conduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, disgorgement, monetary fines, imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our product candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Our business is subject to complex and evolving U.S. and foreign laws and regulations relating to privacy and data protection. These laws and regulations are subject to change and uncertain interpretation, and could result in claims, changes to our business practices, and monetary penalties, and otherwise may harm our business.

A growing body of increasingly stringent domestic and foreign laws and regulations governs the collection, use, disclosure, transfer and other processing of personal data. Among the most stringent of these is the GDPR, which has also been implemented in the United Kingdom ("UK"). The GDPR imposes stringent requirements for controllers and processors of personal data, including, for example, more robust disclosures to individuals and a

strengthened individual data rights regime, shortened timelines for data breach notifications, limitations on retention of information, increased requirements pertaining to special categories of data, such as health data, and additional obligations when we contract with third-party processors in connection with the processing of the personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Economic Area to the United States and other countries, and a recent decision of the European Union's highest court has made complying with those rules more challenging. In addition, the GDPR provides that European Union member states may adopt further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

The GDPR applies extraterritorially, and we may be subject to the GDPR because of our data processing activities that involve the personal data of individuals residing in the European Union, such as in connection with our clinical trials in France. In addition, we maintain an office in Switzerland, which has privacy and data protection laws and regulations similar to the GDPR. Failure to comply with the requirements of the GDPR and the applicable national data protection laws of the European Union member states may result in fines of up to €20,000,000 or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, bans on processing personal data and other administrative penalties. GDPR regulations may impose additional responsibility and liability in relation to the personal data that we process and we may be required to put in place additional mechanisms to ensure compliance with the new data protection rules.

To comply with the GDPR's restrictions on transfer of personal data out of Europe, we have relied on the Standard Contractual Clauses for personal data transfers approved by the European Commission. However, a July 2020 decision of the European Union's highest court called into question whether the Standard Contractual Clauses can lawfully be used for transfers of personal data from the European Union to the United States and most other non-EU countries. Authorities in Switzerland have similarly raised questions about the viability of the Standard Contractual Clauses.

In addition, it is unclear whether the transfer of personal data from the European Union to the UK will continue to remain lawful under the GDPR in light of Brexit. Pursuant to the post-Brexit trade and cooperation agreement between the UK and the European Union, transfers of personal information from the European Economic Area to the UK are not considered restricted transfers under the GDPR for a period of up to six months from January 1, 2021. However, unless the European Union Commission makes an adequacy finding with respect to the UK before the end of that period, the UK will be considered a "third country" under the GDPR, and transfers of personal data from the European Union to the UK will require an approved compliance mechanism to render such transfers lawful under the GDPR. Uncertainty remains regarding how data transfers to and from the UK will be regulated.

If we are unable to implement safeguards necessary to ensure that our transfers of personal data from and within Europe are lawful, we will face increased exposure to regulatory actions, substantial fines and bans on processing personal data from Europe. In addition, we may be required to increase our data processing capabilities in Europe at significant expense. Inability to import personal data from Europe may also restrict our clinical trials activities in France and elsewhere in the region and limit our ability to collaborate with contract research organizations, service providers, contractors and other companies subject to European data protection laws. Additionally, other countries outside of Europe have enacted or are considering enacting similar cross-border data transfer restrictions and laws requiring local data residency, which could increase the cost and complexity of operating our business.

Privacy laws in the United States are also increasingly complex and changing rapidly. For example, the California legislature enacted the California Consumer Privacy Act (“CCPA”), which took effect on January 1, 2020. The CCPA requires covered companies to provide new disclosures to California residents and honor their requests to access, delete and opt-out of certain sharing of their personal data. The CCPA provides for civil penalties for violations and statutory damages for certain data breaches. Since the enactment of the CCPA, new privacy and data security laws have been proposed in more than half of U.S. states, reflecting a trend toward more stringent privacy legislation in the United States. The CCPA itself will expand substantially as a result of California voters approving a November 2020 ballot measure that adopted the California Privacy Rights Act of 2020, which will, among other things, create a new administrative agency to implement and enforce California’s privacy laws effective January 1, 2023. While certain clinical trial activities are exempt from the CCPA’s requirements, other personal information that we handle may be subject to the CCPA, which may increase our compliance costs, exposure to regulatory enforcement action and other liabilities.

The GDPR, CCPA and many other laws and regulations relating to privacy and data protection are still being tested in courts, and they are subject to new and differing interpretations by courts and regulatory officials. We are working to comply with the privacy and data protection laws and regulations that apply to us, and we anticipate needing to devote significant additional resources to complying with these laws and regulations. It is possible that the GDPR, CCPA or other laws and regulations relating to privacy and data protection may be interpreted and applied in a manner that is inconsistent from jurisdiction to jurisdiction or inconsistent with our current policies and practices.

Our actual or perceived failure to adequately comply with applicable laws and regulations relating to privacy and data protection, or to protect personal data and other data we process or maintain, could result in regulatory fines and bans on processing personal information, investigations and enforcement actions, penalties and other liabilities, claims for damages by affected individuals, and damage to our reputation, any of which could materially affect our business, financial condition, results of operations and growth prospects.

The withdrawal of the UK from the European Union, commonly referred to as “Brexit,” may adversely impact our ability to obtain regulatory approvals of our product candidates in the European Union, result in restrictions or imposition of taxes and duties for importing our product candidates into the European Union, and may require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the European Union.

Following the result of a referendum in 2016, the UK left the European Union on January 31, 2020, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the UK and the European Union, the UK was subject to a transition period until December 31, 2020 (“Transition Period”), during which European Union rules continued to apply. A trade and cooperation agreement (“Trade and Cooperation Agreement”) that outlines the future trading relationship between the UK and the European Union was agreed to in December 2020.

Since a significant proportion of the regulatory framework in the UK applicable to our business and our product candidates is derived from European Union directives and regulations, Brexit has had, and will continue to have, a material impact on the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the UK or the European Union. For example, the UK is no longer covered by the centralized procedures for obtaining European Union-wide marketing authorization from the EMA and a separate marketing authorization will be required to market our product candidates in the UK. It is currently unclear whether the Medicines & Healthcare products Regulatory Agency in the UK is sufficiently prepared to handle the increased volume of MAAs it is likely to receive. Any delay in obtaining, or an inability to obtain, any marketing approvals would delay or prevent us from commercializing our product candidates in the UK or the European Union and restrict our ability to generate revenue and achieve and sustain profitability.

While the Trade and Cooperation Agreement provides for the tariff-free trade of medicinal products between the UK and the European Union, there may be additional non-tariff costs to such trade that did not exist prior to the end of the Transition Period. Further, should the UK diverge from the European Union from a regulatory

perspective in relation to medicinal products, tariffs could be put into place in the future. We could therefore, both now and in the future, face significant additional expenses to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the UK. It is also possible that Brexit may negatively affect our ability to attract and retain employees, particularly those from the European Union.

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

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

- decreased demand for our product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulatory authorities;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any product candidate; or
- a decline in our share price.

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We currently carry an aggregate of up to \$10 million of product liability insurance covering our clinical trials. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. If we determine that it is prudent to increase our product liability coverage due to the commercial launch of any approved product, we may be unable to obtain such increased coverage on acceptable terms, or at all. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

Risks Related to Our Reliance on Third Parties

We depend on intellectual property licensed from third parties and termination of any of these licenses could result in the loss of significant rights, which would harm our business.

We are dependent on patents, know-how and proprietary technology, both our own and licensed from others. We entered into an assignment and license agreement with Shire pursuant to which we were assigned exclusive global rights to license intellectual property and know-how related to maralixibat and volixibat, rights to license know-how related to maralixibat from Pfizer and certain patents and know-how related to maralixibat and volixibat from Satiogen. We have in-licensed certain patents and know-how related to volixibat from Shire and Sanofi. We are required to use commercially reasonable efforts or diligent efforts to commercialize products based on the licensed rights and to pay certain royalties based off our net sales and, in the case of Satiogen, our sublicensing revenues. We may not meet these requirements, which could result in a loss or termination of any rights under such agreements. Any termination of these licenses will result in the loss of significant rights and will restrict our ability to commercialize our product candidates.

We are generally also subject to all of the same risks with respect to protection of intellectual property that we license, as we are for intellectual property that we own, which are described below under “Risks Related to Our Intellectual Property.” If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize products could suffer.

We rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates.

We currently rely on, and intend to continue relying on, third-party CROs in connection with our clinical trials for maralixibat and volixibat. We control or will control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with applicable protocol, legal, regulatory and scientific standards, and our reliance on our CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these CROs fail to comply with applicable GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. Upon inspection, such regulatory authorities may not determine that any of our clinical trials comply with the GCP regulations. In addition, our clinical trials must be conducted with drug product produced under cGMP regulations and will require a large number of test subjects. Our failure or any failure by our CROs to comply with these regulations or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of our CROs violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Our CROs are not our employees and, except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our ongoing preclinical, clinical and non-clinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could affect their performance on our behalf. If our CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced 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 other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval for or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Switching or adding CROs involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can

materially impact our ability to meet our desired clinical development timelines. Although we carefully manage our relationships with our CROs, we may encounter challenges or delays in the future and these delays or challenges may have a material adverse impact on our business, prospects, financial condition and results of operations.

In addition, quarantines, shelter-in-place and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, related to COVID-19 or other infectious diseases could impact personnel at our CROs, which could disrupt our clinical timelines, which could have a material adverse impact on our business, prospects, financial condition and results of operations.

We rely completely on third parties to manufacture our preclinical and clinical drug supplies and we intend to rely on third parties to produce commercial supplies of each of our product candidates, if approved, and these third parties may fail to obtain and maintain regulatory approval for their facilities, fail to provide us with sufficient quantities of drug product or fail to do so at acceptable quality levels or prices.

We do not currently have nor do we plan to acquire the infrastructure or capability internally to manufacture our clinical drug supplies for use in the conduct of our clinical trials, and we lack the resources and the capability to manufacture our product candidates on a clinical or commercial scale. Instead, we rely on contract manufacturers for such production. In particular, we rely on a number of different manufacturers to obtain our supply of maralixibat and volixibat to support our clinical trial programs.

We do not currently have any long-term agreement with a manufacturer to produce raw materials, active pharmaceutical ingredients (“APIs”) and the finished products of our product candidates or the associated packaging used in our current product formats. We will need to identify and qualify a third-party manufacturer prior to commercialization of our product candidates, and we intend to enter into agreements for commercial production with third-party suppliers. As our product candidates are intended to treat rare liver diseases, we will only require a low-volume of raw materials and APIs, and in the case of maralixibat and volixibat, in some cases with single-source suppliers and manufacturers. Our reliance on third-party suppliers and manufacturers, including single-source suppliers, could harm our ability to develop our product candidates or to commercialize any product candidates that are approved. Further, any delay in identifying and qualifying a manufacturer for commercial production could delay the potential commercialization of our product candidates, and, in the event that we do not have sufficient product to complete our planned clinical trials, it could delay such trials. The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the applicable regulatory authorities, including the FDA, pursuant to inspections that will be conducted after an NDA or comparable foreign regulatory marketing application is submitted. We do not control the manufacturing process of our product candidates and are completely dependent on our contract manufacturing partners for compliance with the FDA’s cGMP requirements for manufacture of both the active drug substances and finished drug product. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the FDA’s strict regulatory requirements, they will not be able to secure or maintain FDA approval for the manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or any other applicable regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, or if our suppliers or contract manufacturers decide they no longer want to supply or manufacture for us, we may need to find alternative manufacturing facilities, in which case we might not be able to identify manufacturers for clinical or commercial supply on acceptable terms, or at all, which would significantly impact our ability to develop, obtain regulatory approval for or market maralixibat and volixibat.

In addition, the manufacture of pharmaceutical products is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up and validating initial production and absence of contamination. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, operator error, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. Furthermore, if contaminants are discovered in our supply of maralixibat or volixibat or in the manufacturing facilities, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. Any stability or other issues relating to the manufacture of our product candidates may occur in the future. In addition, quarantines, shelter-in-place and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, related to COVID-19 or other infectious diseases could impact personnel at our third-party manufacturing facilities upon which we rely, or the availability or cost of materials, which could disrupt the supply chain for our product candidates. Further, our manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our manufacturers were to encounter any of these difficulties, or otherwise fail to comply with their contractual obligations, our ability to provide our product candidate to patients in clinical trials would be jeopardized. Any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely.

Further, we are in the process of switching or adding contract manufacturing organizations for both maralixibat and volixibat, which is cost-intensive and time-consuming. The success of these transfers is necessary for continuous supply to clinical trials and potential future commercial demand.

The actions of distributors and specialty pharmacies could affect our ability to sell or market products profitably. Fluctuations in buying or distribution patterns by such distributors and specialty pharmacies could adversely affect our revenues, financial condition, or results of operations.

If maralixibat is approved, we intend to rely on specialty pharmacies or distributors for a considerable portion of product sales. The failure of one or more of these parties could adversely affect our revenues, financial condition or results of operations. Our revenues, financial condition or results of operations may also be affected by fluctuations in buying or distribution patterns of one or more of these parties. These fluctuations may also result from seasonality, pricing, wholesaler inventory objectives, or other factors, including the effects of the COVID-19 pandemic. The COVID-19 pandemic may increase the proportion of uninsured patients in the United States, which may increase utilization of our patient assistance or free drug program.

Risks Related to Our Financial Position and Capital Requirements

We will need substantial additional financing to develop our product candidates and implement our operating plans. If we fail to obtain additional financing, we may be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts to continue the clinical development and seek regulatory approval of our product candidates. We will require significant additional amounts in order to prepare for commercialization, and, if approved, to launch and commercialize our product candidates.

Based on our current and anticipated level of operations, we believe our cash, cash equivalents and investments, will be sufficient to fund current operations through at least the next 12 months. However, changing circumstances may cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. We will require additional capital for the further development and commercialization of our product candidates and may need to raise additional funds sooner if we choose to expand more rapidly than we presently anticipate. In addition, in the third quarter of 2020, we initiated an expanded access program for maralixibat in ALGS in the United States and Canada,

and we are also planning a similar program in other countries, all of which requires additional resources and costs to support.

Additional funding may not be available on acceptable terms, or at all. As a result of the COVID-19 pandemic and actions taken to slow its spread, the global credit and financial markets have experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. If the equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of maralixibat or volixibat or other research and development initiatives. We also could be required to seek collaborators for our product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to our product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves.

Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

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.

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire 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 strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms unfavorable to us.

If we raise additional funds through collaboration, strategic partnerships and licensing arrangements with third parties, such as the Revenue Interest Purchase Agreement (“RIPA”) with Mulholland SA LLC, an affiliate of Oberland Capital LLC, as agent for purchasers party thereto (the “Purchasers”), and the Purchasers, we may have to relinquish valuable rights to maralixibat, our intellectual property, future revenue streams or grant licenses on terms that are not favorable to us. For instance, as part of the RIPA, the Purchasers have the right to receive certain revenue interests from us based on the net sales of maralixibat, once approved, and we have granted the Purchasers a senior security interest in certain of our assets. If our cash flows and capital resources are insufficient to allow us to make required payments, we may have to reduce or delay capital expenditures, sell assets or seek additional capital.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. As of December 31, 2020, we had federal and state net operating loss (“NOL”) carryforwards of approximately \$123.5 million and \$2.6 million, respectively. The federal NOL carryforwards do not expire, and the state NOL carryforwards will begin to expire in 2038, unless previously utilized. We also have federal and state research and development credit carryforwards totaling \$14.5 million and \$0.9 million, respectively. The federal research and development credit carryforwards will begin to expire in 2038, unless previously utilized. The state research and development credits will not expire.

Under the Tax Act, as modified by the Coronavirus Aid, Relief, and Economic Security Act (“CARES Act”), federal NOLs generated in taxable years beginning after December 31, 2017 may be carried forward indefinitely, but the deductibility of such federal NOLs in taxable years beginning after December 31, 2020 is limited to 80% of taxable income. It is uncertain if and to what extent various states will conform to the Tax Act or the CARES Act.

Our NOL carryforwards and other applicable tax attributes are subject to review and possible adjustment by the U.S. Internal Revenue Service and state tax authorities and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50 percentage points (by value), as defined under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended. It is possible that we have experienced one or more such ownership changes in the past, and we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership. We may therefore be limited in the portion of NOL carryforwards and other applicable tax attributes that we can use in the future to offset future taxable income. In addition, at the state level, there may be periods during which the use of net operating losses is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For example, on June 29, 2020, California enacted AB 85, which imposed limits on the usability of California state net operating losses and certain tax credits in tax years beginning after 2019 and before 2023. We have recorded a full valuation allowance related to our NOLs and other deferred tax assets due to the uncertainty of the ultimate realization of the future benefits of those assets.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, or if the scope of the intellectual property protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our product candidates, if approved, may be adversely affected.

Our commercial success will depend in part on obtaining and maintaining a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our technologies. Any unauthorized disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

The patent positions of biotechnology and pharmaceutical companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States or in many jurisdictions outside of the United States. Changes in either the patent laws or interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be enforced in the patents that may be issued from the applications we currently or may in the future own or license from third parties. Further, if any patents we obtain or license are deemed invalid and unenforceable, our ability to commercialize or license our technology could be adversely affected.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our actual or potential future collaborators will be successful in protecting our product candidates, proprietary technologies and their uses by obtaining and defending patents. These risks and uncertainties include the following:

- the United States Patent and Trademark Office (“USPTO”) and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- patent applications may not result in any patents being issued;
- patents that may be issued or in-licensed may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use and sell our potential product candidates;
- other parties may have designed around our claims or developed technologies that may be related or competitive to our platform, may have filed or may file patent applications and may have received or may receive patents that overlap or conflict with our patent applications, either by claiming the same methods or devices or by claiming subject matter that could dominate our patent position;
- any successful opposition to any patents owned by or licensed to us could deprive us of rights necessary for the practice of our technologies or the successful commercialization of any products or product candidates that we may develop;
- because patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we or our licensors were the first to file any patent application related to our product candidates, proprietary technologies and their uses;
- an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications for any application with an effective filing date before March 16, 2013;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

The patent prosecution process is also expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. We may also rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or feasible. However, trade secrets are difficult to protect. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. If we do not adequately protect our intellectual property and proprietary technology, competitors may be able to use our product candidates and proprietary technologies and erode or negate any competitive advantage we may have, which could have a material adverse effect on our financial condition and results of operations. For example:

- others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of our patents;
- we might not have been the first to make the inventions covered by our pending patent applications;
- we might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- any patents that we obtain may not provide us with any competitive advantages;
- we may not develop additional proprietary technologies that are patentable;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we cannot ensure that any of our patents, or any of our pending patent applications, if issued, or those of our licensors, will include claims having a scope sufficient to protect our products;
- we cannot ensure that we will be able to successfully commercialize our products on a substantial scale, if approved, before the relevant patents that we own or license expire; or
- the patents of others may have an adverse effect on our business.

Others have filed, and in the future are likely to file, patent applications covering products and technologies that are similar, identical or competitive to ours or important to our business. We cannot be certain that any patent application owned by a third party will not have priority over patent applications filed or in-licensed by us, or that we or our licensors will not be involved in interference, opposition or invalidity proceedings before U.S. or non-U.S. patent offices.

We cannot be certain that the claims in our issued patents and pending patent applications covering maralixibat or volixibat will be considered patentable by the USPTO, courts in the United States, or by patent

offices and courts in foreign countries. Furthermore, the laws of some foreign countries do not protect 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.

The strength of patents in the biotechnology and pharmaceutical fields involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover maralixibat or volixibat in the United States or in foreign countries. Even if such patents do successfully issue, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Any successful opposition to our patents could deprive us of exclusive rights necessary for the successful commercialization of maralixibat or volixibat. Furthermore, even if they are unchallenged, our patents may not adequately protect our intellectual property, provide exclusivity for maralixibat or volixibat or prevent others from designing around our claims. If the breadth or strength of protection provided by the patents we hold with respect to maralixibat or volixibat is threatened, it could dissuade companies from collaborating with us to develop, or threaten our ability to commercialize, maralixibat or volixibat.

Further, if we encounter delays in our development efforts, including our clinical trials, the period of time during which we could market maralixibat or volixibat under patent protection would be reduced. In addition, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however the life of a patent, and the protection it affords, is limited. A patent term extension of up to five years based on regulatory delay may be available in the United States under the Hatch-Waxman Act. However, only a single patent can be extended for each marketing approval, and any patent can be extended only once, for a single product. Moreover, the scope of protection during the period of the patent term extension does not extend to the full scope of the claim, but instead only to the scope of the product as approved. Further, a patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Laws governing analogous patent term extensions in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Additionally, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced.

For U.S. patent applications in which claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our participation in an interference proceeding may fail and, even if successful, may result in substantial costs and distract our management and other employees.

For U.S. patent applications containing a claim not entitled to priority before March 16, 2013, there is greater level of uncertainty in the patent law. In September 2011, the Leahy-Smith America Invents Act, or America Invents Act, was signed into law. The America Invents Act includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The USPTO is developing regulations and procedures to govern the administration of the America Invents Act, and many of the substantive changes to patent law associated with the America Invents Act, and in particular, the “first to file” provisions, were enacted on March 16, 2013. It remains unclear what impact the America Invents Act will have on the operation of our business. Moreover, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidates and drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect. We require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology, such as third parties involved in the manufacture of our product candidates, such as maralixibat and volixibat, and third parties involved in our clinical trials to enter into confidentiality agreements. We cannot be certain that all such agreements have been duly executed, that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results and financial condition.

We currently rely on method-of-use and formulation patents to protect maralixibat and composition-of-matter and method-of-use patents to protect volixibat.

We currently have rights to patent applications in the United States, Europe and other countries covering the methods of treating cholestatic liver diseases using ASBTs, including maralixibat and volixibat, with limited systemic exposure. We also have rights to patent applications in Europe and other countries covering the use of compositions of such ASBTs in treating pediatric cholestatic liver diseases. A patent based on any of these patent applications may never be issued. We do not have patents or patent applications covering maralixibat as a composition-of-matter. Therefore, the primary patent-based intellectual property protection for our maralixibat program will be any patents granted on the pending method-of-use and formulation patent applications.

Composition-of-matter patents on active pharmaceutical ingredients are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection without regard to any method of use. Method-of-use patents protect the use of a product for the specified method. Method-of-use patents do not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their products for our targeted indication(s), physicians may prescribe these products "off-label." Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute.

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

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent process. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on any issued patents and/or applications are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay these fees due to foreign patent agencies. While an inadvertent lapse may sometimes 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. In such an event, our competitors might be able to enter the market earlier than should otherwise have been the case, which would have a material adverse effect on our business.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly on obtaining and enforcing patents. Our patent rights may be affected by developments or uncertainty in U.S. or foreign patent statutes, patent case law, USPTO rules and regulations or the rules and regulations of foreign patent offices. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States may, at any time, enact changes to U.S. patent law and regulations, including by legislation, by regulatory rule-making, or by judicial precedent, that adversely affect the scope of patent protection available and weakened the rights of patent owners to obtain patents, enforce patent infringement and obtain injunctions and/or damages. For example, the scope of patentable subject matter under 35 U.S.C. 101 has evolved significantly over the past several years as the Court of Appeals for the Federal Circuit and the Supreme Court issued various opinions, and the USPTO modified its guidance for practitioners on multiple occasions. Other countries may likewise enact changes to their patent laws in ways that adversely diminish the scope of patent protection and weaken the rights of patent owners to obtain patents, enforce patent infringement and obtain injunctions and/or damages. Further, the United States and other governments may, at any time, enact changes to law and regulation that create new avenues for challenging the invalidity of issued patents. For example, the America Invents Act created new administrative post-grant proceedings, including post-grant review, inter partes review, and derivation proceedings that allow third parties to challenge the validity of issued patents. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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

Patents are of national or regional effect. Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive. In addition, the laws of some foreign countries do not protect intellectual property rights in the same manner and to the same extent as laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement of such patent protection is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

The requirements for patentability may differ in certain countries. For example, unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. In India, unlike the United States, there is no link between regulatory approval for a drug and its patent status. In addition to India, certain countries in Europe and developing countries, including China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we may have limited remedies if patents are infringed or if we are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology or pharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention

from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are a party to a number of license agreements under which we are granted intellectual property rights that are important to our business. For example, certain trade secrets related to maralixibat are licensed from Pfizer, and patents, patent applications and trade secrets related to volixibat are licensed from Sanofi. Our existing license agreements as related to maralixibat and volixibat impose various development, regulatory and/or commercial diligence obligations, payment of milestones and/or royalties and other obligations. If we fail to comply with our obligations under a license agreement, or we are subject to a bankruptcy, the license agreement may be terminated, in which event we would not be able to develop, commercialize or market maralixibat or volixibat, as the case may be.

Licensing of intellectual property rights is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property rights subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property rights of the licensor that are not subject to the licensing agreement;
- our right to sublicense intellectual property rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property rights that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, our business, results of operations, financial condition and prospects may be adversely affected. We may enter into additional licenses in the future and if we fail to comply with obligations under those agreements, we could suffer adverse consequences.

We may become subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may be subject to claims that former employees (including former employees of our licensors), collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our product candidates or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and/or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property

rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We may not be successful in obtaining or maintaining necessary rights to product components and processes for our development pipeline through acquisitions and in-licenses.

Presently we have intellectual property rights, through licenses from third parties including Shire, Pfizer, Satiogen and Sanofi, related to our product candidates. For example, we have our license agreements with Shire and Satiogen for both maralixibat and volixibat. We have our license agreement with Shire, Satiogen and Pfizer for our intellectual property rights covering maralixibat. Further, we have our license agreement with Sanofi for our intellectual property rights covering volixibat. Because our programs may require the use of additional proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights. In addition, our product candidates may require specific formulations to work effectively and efficiently and these rights may be held by others. We may be unable to acquire or in-license proprietary rights related to any compositions, formulations, methods of use, processes or other intellectual property rights from third parties that we identify as being necessary for our product candidates. Even if we are able to obtain a license to such proprietary rights, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

Where we obtain licenses from or collaborate with third parties, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties, or such activities, if controlled by us, may require the input of such third parties. We may also require the cooperation of our licensors and collaborators to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business, in compliance with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such application. Moreover, if we do obtain necessary licenses, we will likely have obligations under those licenses, including making royalty and milestone payments, and any failure to satisfy those obligations could give our licensor the right to terminate the license. Termination of a necessary license, or expiration of licensed patents or patent applications, could have a material adverse impact on our business. Our business would suffer if any such licenses terminate, if the licensors fail to abide by the terms of the license, if the licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. Furthermore, if any licenses terminate, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties may gain the freedom to seek regulatory approval of, and to market, products identical to ours. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

The licensing and acquisition of third-party proprietary rights is a competitive area, and companies, which may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party proprietary rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

For example, we may collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate an exclusive license to any of the institution's proprietary rights in technology resulting from the collaboration. Regardless of such option to negotiate a license, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to us. If we are unable to do so, the institution may offer, on an exclusive basis, their proprietary rights to other parties, potentially blocking our ability to pursue our program.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us, either on reasonable terms, or at all. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment, or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights on commercially reasonable terms, our ability to commercialize our products, and our business, financial condition and prospects for growth could suffer.

Third-party claims alleging intellectual property infringement may prevent or delay our drug discovery and development efforts.

Our success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including inter partes review, interference and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. The America Invents Act introduced new procedures including inter partes review and post grant review. The implementation of these procedures brings uncertainty to the possibility of challenges to our patents in the future and the outcome of such challenges. 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 our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our activities related to our product candidates may give rise to claims of infringement of the patent rights of others.

The pharmaceutical and biotechnology industries have produced a proliferation of patents, and it is not always clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. We cannot assure you that any of our current or future product candidates will not infringe existing or future patents. We may not be aware of patents that have already issued that a third party might assert are infringed by one of our current or future product candidates. Nevertheless, we are not aware of any issued patents that will prevent us from marketing our product candidates.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents of which we are currently unaware 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 and may be confidential for 18 months or more after filing, there may be currently pending third-party patent applications which may later result in issued patents that our product candidates or our technologies may infringe, or which such third parties claim are infringed by the use of our technologies. Parties making claims against us for infringement or misappropriation of their intellectual property rights may seek and 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, could involve substantial expenses and could be a substantial diversion of employee resources from our business.

If we collaborate with third parties in the development of technology in the future, our collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation or potential liability. Further, collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability. In the future, we may agree to indemnify our commercial collaborators against certain intellectual property infringement claims brought by third parties.

Any claims of patent infringement asserted by third parties would be time consuming and could:

- result in costly litigation;
- divert the time and attention of our technical personnel and management;
- cause development delays;

- prevent us from commercializing maralixibat or our other product candidates until the asserted patent expires or is held finally invalid or not infringing in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis;
- require us to pay damages to the party whose intellectual property rights we may be found to be infringing, which may include treble damages if we are found to have been willfully infringing such intellectual property;
- require us to pay the attorney's fees and costs of litigation to the party whose intellectual property rights we may be found to be infringing; and/or
- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all.

If we are sued for patent infringement, we would need to demonstrate that our products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid, and we may not be able to do either. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and divert management's time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, which may not be available, defend an infringement action or challenge the validity of the patents in court. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to defend an infringement action successfully or have infringed patents declared invalid, we may incur substantial monetary damages, encounter significant delays in bringing our product candidates to market and be precluded from manufacturing or selling our product candidates.

We do not always conduct independent reviews of pending patent applications of and patents issued to third parties. We cannot be certain that others have not filed patent applications for technology covered by our pending applications, or that we were the first to invent the technology, because:

- some patent applications in the United States may be maintained in secrecy until the patents are issued;
- patent applications in the United States and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived;
- pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our product candidates or the use of our product candidates;
- identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims;
- patent applications in the United States are typically not published until 18 months after the priority date; and
- publications in the scientific literature often lag behind actual discoveries.

Furthermore, the scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history and can involve other factors such as expert opinion. Our interpretation of the relevance or the scope of claims in a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. Further, we may incorrectly determine that our technologies, products, or product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending patent application will issue with claims of relevant scope. Our determination of the expiration date of any patent in

the United States or internationally that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our products or product candidates.

Our competitors may have filed, and may in the future file, patent applications covering technology similar to ours, and others may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our product candidates and future approved products or impair our competitive position. Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. 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. Any such patent application may have priority over our patent applications, which could further require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to ours, we may have to participate in an interference proceeding declared by the USPTO to determine priority of invention in the United States. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful if, unbeknownst to us, the other party had independently arrived at the same or similar invention prior to our own invention, resulting in a loss of our U.S. patent position with respect to such inventions. Other countries have similar laws that permit secrecy of patent applications and may be entitled to priority over our applications in such jurisdictions.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations.

If a third party prevails in a patent infringement lawsuit against us, we may have to stop making and selling the infringing product, pay substantial damages, including treble damages and attorneys' fees if we are found to be willfully infringing a third party's patents, obtain one or more licenses from third parties, pay royalties or redesign our infringing 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. 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 our product candidates, which could harm our business significantly. Even if we were able to obtain a license, the rights may be nonexclusive, which may give our competitors access to the same intellectual property.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industries, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other pharmaceutical companies including our competitors or potential competitors. We may become subject to claims that we, our employees or consultants inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team and other employees.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful. Further, our issued patents could be found invalid or

unenforceable if challenged in court, and we may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights.

Third parties including competitors may infringe, misappropriate or otherwise violate our patents, patents that may issue to us in the future, or the patents of our licensors that are licensed to us. To counter infringement or unauthorized use, we may need to or choose to file infringement claims, which can be expensive and time-consuming. 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.

If we choose to go to court to stop another party from using the inventions claimed in our patents, that individual or company has the right to ask the court to rule that such patents are invalid, unenforceable, or should not be enforced against that third party for any number of reasons. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements for patentability, including lack of novelty, obviousness, lack of written description, indefiniteness, or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution, i.e. committed inequitable conduct. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. Similar mechanisms for challenging the validity and enforceability of a patent exist in foreign patent offices and courts and may result in the revocation, cancellation, or amendment of any foreign patents we or our licensors hold now or in the future. The outcome following legal assertions of invalidity and unenforceability is unpredictable, and prior art could render our patents or those of our licensors invalid. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. Such a loss of patent protection would have a material adverse impact on our business.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our product candidates to market.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

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

Our ability to enforce our patent rights depends on our ability to detect infringement. It may be difficult to detect infringers who do not advertise the components or methods that are used in connection with their products

and services. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product or service. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

Because of the expense and uncertainty of litigation, we may not be in a position to enforce our intellectual property rights against third parties.

Because of the expense and uncertainty of litigation, we may conclude that even if a third party is infringing our issued patent, any patents that may be issued as a result of our pending or future patent applications or other intellectual property rights, the risk-adjusted cost of bringing and enforcing such a claim or action may be too high or not in the best interest of our company or our stockholders. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

We rely on trade secrets to protect our proprietary technologies, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors, and inventions agreements with employees, consultants and advisors, to protect our trade secrets and other proprietary information. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using commonly accepted physical and technological security measures. Despite these efforts, we cannot provide any assurances that all such agreements have been duly executed, and these agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

In addition, such security measures may not provide adequate protection for our proprietary information, for example, in the case of misappropriation of a trade secret by an employee, consultant, customer or third party with authorized access. Our security measures may not prevent an employee, consultant or customer from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our products that we consider proprietary. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and time-consuming, and the outcome is unpredictable. Even though we use commonly accepted security measures, the criteria for protection of trade secrets can vary among different jurisdictions.

Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. Trade secrets will over time be disseminated within the industry through independent development, the publication of journal articles and the movement of personnel skilled in the art from company to company or academic to industry scientific positions. Though our agreements with third parties typically restrict the ability of our advisors, employees, collaborators, licensors, suppliers, third-party contractors and consultants to publish data potentially relating to our trade secrets, our agreements may contain certain limited publication rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Because from time to time we expect to rely on third parties in the development, manufacture, and distribution of our products and provision of our services, we must, at times, share trade secrets with them. Despite employing the contractual and other security precautions described above, the need to share trade secrets increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced and our competitive position would be harmed. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our current or future trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

Moreover, any name we have proposed to use with any of our product candidates in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark.

Similar requirements exist in Europe. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed proprietary product names, it may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. If we assert trademark infringement claims, a

court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our products.

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include that:

- collaborators have significant discretion in determining the efforts and resources that they will apply to collaborations;
- collaborators may not pursue development and commercialization of our products or may elect not to continue or renew development or commercialization programs based on trial or test results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates;
- a collaborator with marketing, manufacturing and distribution rights to one or more products may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that causes the delay or termination of the research, development or commercialization of our current or future products or that results in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated, and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable current or future products;
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property; and
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

Risks Related to Ownership of Our Common Stock

The trading price of our common stock may be volatile, and you could lose all or part of your investment.

The trading price of our common stock is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. For example, the closing price of our common stock since its trading began on July 18, 2019 and to March 8, 2021 has ranged from a low of \$6.84 to a high of \$26.59. In addition to the factors discussed in this "Risk Factors" section, these factors include:

- any delay in our regulatory filings for maralixibat or volixibat and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;
- our failure to commercialize our product candidates;
- the commencement, enrollment or results of our ongoing clinical trials of maralixibat and volixibat or any future clinical trials we may conduct, or changes in the development status of our product candidates;
- adverse results or delays in clinical trials;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- adverse regulatory decisions, including failure to receive regulatory approval for our product candidates;
- changes in laws or regulations applicable to our product candidates, including but not limited to clinical trial requirements for approvals;
- changes in the structure of health care payment systems;
- the failure to obtain coverage and adequate reimbursement of our product candidates, if approved;
- adverse developments concerning our manufacturers;
- our inability to obtain adequate product supply for any approved drug product or inability to do so at acceptable prices;
- our inability to establish collaborations if needed;
- management transitions and additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to the use of our product candidates;
- introduction of new products or services offered by us or our competitors;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- our ability to effectively manage our growth;
- the size and growth, if any, of the markets for PFIC, ALGS and other cholestatic liver diseases that we may target;
- our ability to successfully enter new markets or develop additional product candidates;
- actual or anticipated variations in quarterly operating results;
- our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- changes in the market valuations of similar companies;
- overall performance of the equity markets;

- issuances of debt or equity securities;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- changes in accounting practices;
- ineffectiveness of our internal controls;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- general political, health and economic conditions, including the COVID-19 pandemic; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and Nasdaq-listed and biopharmaceutical companies in particular, 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. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources, which would harm our business, operating results or financial condition.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We have never declared or paid any cash dividend on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

Our principal stockholders and management own a significant percentage of our stock and are able to exert significant control over matters subject to stockholder approval.

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

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of December 31, 2020, there were 29,776,544 shares of our common stock outstanding, excluding 256,056 shares subject to repurchase, as described in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our employee benefit plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, Rule 144 and Rule 701 under the Securities Act of 1933, as amended

("Securities Act"). If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Further, certain holders of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates, as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

Our payment obligations under the RIPA may adversely affect our financial position or results of operations and our ability to raise additional capital which in turn may increase our vulnerability to adverse regulatory developments or economic or business downturns.

As described in “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and Capital Resources,” on December 8, 2020, we entered into the RIPA. Pursuant to the RIPA, the Purchasers paid us \$50.0 million on closing, less certain transaction expenses. We may also be entitled to receive up to approximately \$150.0 million in subsequent installments as follows: (i) \$65.0 million if the FDA has accepted for review our NDA for maralixibat as a treatment for cholestatic pruritus due to ALGS on or prior to a specified date; (ii) \$35.0 million if the FDA has approved maralixibat as a treatment for ALGS on or prior to a specified date; and (iii) up to \$50.0 million at the option of the Purchasers to finance in-licenses or other acquisitions. As consideration for such payments, the Purchasers will have a right to receive certain revenue interests (the “Revenue Interests”) from us based on annual net sales of maralixibat, if approved, which will be tiered payments (the “Revenue Interest Payments”) based on whether such annual net sales are (i) less than or equal to \$350.0 million (“Tier 1”), (ii) exceeding \$350.0 million and less than or equal to \$1.1 billion (“Tier 2”), or (iii) exceeding \$1.1 billion (“Tier 3”). The Revenue Interest Payments will initially be 9.75% (at Tier 1) and 2.00% (at Tier 2 and Tier 3) of such annual net sales in a specified territory (the “Covered Territory”); provided that (i) if the Purchasers have received Revenue Interest Payments in an amount equal to or greater than 110.0% of the total payments actually made by the Purchasers to us, exclusive of transaction expenses (the “Cumulative Purchaser Payments”), on or prior to December 31, 2026, the Revenue Interests shall be reduced to 2.00% at Tier 1 and 0.00% at Tier 3 for all subsequent calendar years beginning on January 1, 2027 and (ii) if the Purchasers have not received Revenue Interest Payments in an amount equal to or greater than 110.0% of the Cumulative Purchaser Payments on or prior to December 31, 2026, the Revenue Interests shall be increased for all subsequent calendar years beginning on January 1, 2027 to a single defined rate (with no separate tiers) that would have provided the Purchasers with an amount equal to 110.0% of the Cumulative Purchaser Payments on or prior to December 31, 2026 had such rate applied to Tier 1 of initial Revenue Interest Payments. The Purchasers’ rights to receive the Revenue Interest Payments shall terminate on the date on which the Purchasers have received Revenue Interest Payments of 195.0% of the Cumulative Purchaser Payments, unless the RIPA is terminated earlier. The RIPA and the revenue interest stream payable to the Purchasers could have important negative consequences to the holders of our securities. For example, a portion of our cash flow from operations will be needed to pay certain revenue interests to the Purchasers and will not be available to fund future operations. Additionally, we may have increased vulnerability to adverse general economic and industry conditions. Payment requirements under the RIPA will increase our cash outflows. Our future operating performance is subject to market conditions and business factors that are beyond our control. If our cash inflows and capital resources are insufficient to allow us to make required payments, we may have to reduce or delay capital expenditures, sell assets or seek additional capital. If we raise funds by selling additional equity, such sale would result in dilution to our stockholders. If we are required to secure funding, we may not be able to do so on terms acceptable to us, or at all. Failure to pay certain amounts to the Purchasers when due would result in a default under the RIPA and result in foreclosure on certain of our assets which would have a material adverse effect on our operations and financial condition. The RIPA contains customary affirmative and negative non-financial covenants and events of default, including covenants and restrictions that, among other things, grant a senior security interest in our assets and restrict our ability to incur liens, incur additional indebtedness, make loans and investments, engage in mergers and acquisitions, and engage in asset sales. Additionally, the Purchasers under the RIPA have an option (the “Put Option”) to terminate the RIPA and to require us to repurchase future Revenue Interests upon enumerated events such as a bankruptcy event, an uncured material breach, a material adverse effect (which can include adverse developments related to the regulatory approval of our product candidates) or a change of control. The triggering of the Put Option, including by our failure to comply with these covenants, could permit the Purchasers to declare certain amounts to be immediately due and payable. Further, if we are liquidated, the Purchasers’ right to repayment would be senior to the rights of the holders of our common stock. Any triggering of the Put Option or other declaration by the Purchasers of an event of default under the RIPA could significantly harm our financial condition, business and prospects and could cause the price of our common stock to decline.

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

We expect that significant additional capital may be needed in the future to continue our planned operations, including conducting clinical trials, commercialization efforts, expanded research and development activities and costs associated with operating a public company. To raise capital, 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, including through the Shelf Registration. For example, in August 2020, we entered into the Sales Agreement with SVB Leerink, pursuant to which we may elect to issue and sell, from time to time, shares of common stock having an aggregate offering price of up to \$75.0 million under the Shelf Registration through SVB Leerink acting as the sales agent and/or principal. If we sell common stock, convertible securities or other equity securities, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences and privileges senior to the holders of our common stock.

Pursuant to our 2019 Equity Incentive Plan (“2019 Plan”), our management is authorized to grant equity incentive awards to our employees, directors and consultants. We also maintain a 2019 Employee Stock Purchase Plan (“ESPP”) pursuant to which our management is authorized to grant options to purchase shares of our common stock to our employees. In addition, in March 2020, we adopted a 2020 Inducement Plan, pursuant to which our board of directors, or a committee thereof, is authorized to grant inducement awards to new hires as a material inducement to their employment with us.

Additionally, the number of shares of our common stock reserved for issuance under our 2019 Plan is subject to an automatic increase on January 1 of each year through and including January 1, 2029, by 5.0% of the total number of shares of our capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by our board of directors. The number of shares of our common stock reserved for issuance under our ESPP is subject to an automatic increase on January 1 of each year through and including January 1, 2029, by the lesser of (i) 1.0% of the total number of shares of our capital stock outstanding on December 31 of the preceding calendar year, and (ii) 1,500,000 shares of common stock. Unless our board of directors elects not to increase the number of shares available for future grant each year, our stockholders may experience additional dilution, which could cause our stock price to fall.

Our business could be negatively affected as a result of actions of activist stockholders, and such activism could impact the trading value of our securities.

Stockholders may, from time to time, engage in proxy solicitations or advance stockholder proposals, or otherwise attempt to effect changes and assert influence on our board of directors and management. Activist campaigns that contest or conflict with our strategic direction or seek changes in the composition of our board of directors could have an adverse effect on our operating results and financial condition. A proxy contest would require us to incur significant legal and advisory fees, proxy solicitation expenses and administrative and associated costs and require significant time and attention by our board of directors and management, diverting their attention from the pursuit of our business strategy. Any perceived uncertainties as to our future direction and control, our ability to execute on our strategy, or changes to the composition of our board of directors or senior management team arising from a proxy contest could lead to the perception of a change in the direction of our business or instability which may result in the loss of potential business opportunities, make it more difficult to pursue our strategic initiatives, or limit our ability to attract and retain qualified personnel and business partners, any of which could adversely affect our business and operating results. If individuals are ultimately elected to our board of directors with a specific agenda, it may adversely affect our ability to effectively implement our business strategy and create additional value for our stockholders. We may choose to initiate, or may become subject to, litigation as a result of the proxy contest or matters arising from the proxy contest, which would serve as a further distraction to our board of directors and management and would require us to incur significant additional costs. In addition, actions such as those described above could cause significant fluctuations in our stock price based upon temporary or speculative market perceptions or other factors that do not necessarily reflect the underlying fundamentals and prospects of our business.

Our failure to meet Nasdaq's continued listing requirements could result in a delisting of our common stock.

If we fail to satisfy the continued listing requirements of Nasdaq, such as the corporate governance requirements or the minimum closing bid price requirement, Nasdaq may take steps to delist our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the Nasdaq minimum bid price requirement or prevent future non-compliance with the listing requirements of Nasdaq.

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control, which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the chairman of the board of directors, the chief executive officer, the president or by a majority of the total number of authorized directors;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirors to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative action or proceeding brought on our behalf; (ii) any action or proceeding asserting a claim of breach of a fiduciary duty owed by any of our current or former directors, officers or other employees to us or our stockholders; (iii) any action or proceeding asserting a claim against us or any of our current or former directors, officers or other employees, arising out of or pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws; (iv) any action or proceeding to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws; (v) any action or proceeding as to which the Delaware General Corporation Law confers jurisdiction to the Court of Chancery of the State of Delaware; and (vi) any action asserting a claim against us or any of our directors, officers or other employees governed by the internal affairs doctrine, in all cases to the fullest extent permitted by law and subject to the court's having personal jurisdiction over the indispensable parties named as defendants. These provisions would not apply to suits brought to enforce a duty or liability created by the Exchange Act, or any other claim for which the federal courts have exclusive jurisdiction. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

These exclusive-forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees and may discourage these types of lawsuits. If a court were to find either exclusive-forum provision in our amended and restated certificate of incorporation or amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could seriously harm our business.

General Risk Factors

Our computer systems, or those used by our CROs or other contractors or consultants, may fail or suffer cybersecurity incidents and other disruptions, including the theft of our intellectual property.

In the course of our business, we collect, store and transmit proprietary, confidential and sensitive information, including personal information. The information and data processed and stored in our technology systems, and those of our research collaborators, CROs, contractors, consultants and other third parties on which we depend to operate our business, may be vulnerable to security breaches, loss, damage, corruption, unauthorized access, use or disclosure or misappropriation. Such incidents may also result from errors or malfeasance by our personnel or the personnel of the third parties with which we work, malware, viruses, software vulnerabilities, hacking, denial of service attacks, social engineering (including phishing), ransomware, credential stuffing or other cyberattacks, including attacks by state-sponsored organizations or sophisticated groups of hackers.

While we have developed systems and processes designed to protect the integrity, confidentiality and security of the confidential and personal information under our control, we cannot assure you that our security measures or those of the third parties we depend on will be effective in preventing cybersecurity incidents. There are many different and rapidly evolving cybercrime and hacking techniques, and we may be unable to anticipate attempted security breaches, identify them before our information is exploited, or react in a timely manner.

Additionally, as a result of the ongoing COVID-19 pandemic, certain functional areas of our workforce remain in a remote work environment and outside of our corporate network security protection boundaries, which imposes additional risks to our business, including increased risk of industrial espionage, phishing and other cybersecurity attacks and unauthorized dissemination of proprietary or confidential information, any of which could have a material adverse effect on our business.

Although, to our knowledge, we have not experienced a material system failure or cybersecurity incident to date, if such an event were to occur, it could result in a material disruption of our development programs and our business operations, whether due to a loss of trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed, ongoing or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third-party research institution collaborators, CROs, other contractors and consultants for many aspects of our business, including research and development activities and manufacturing of our product candidates, and similar events relating to their computer systems could also have a material adverse effect on our business. Cybersecurity incidents and any unauthorized access or disclosure of our information or intellectual property could also compromise our intellectual property and patent portfolio, expose sensitive business information, expose the personal information of our employees, require us to incur significant remediation costs, disrupt key business operations and divert attention of management and key information technology resources. Such incidents could also subject us to significant liability, harm our competitive position and delay the further development and commercialization of our product candidates.

Our insurance coverage may not be adequate for cybersecurity liabilities, may not continue to be available to us on economically reasonable terms, or at all, and any insurer may deny coverage as to any future claim. The successful assertion of one or more large claims against us that exceed available insurance coverage, or the occurrence of changes in our insurance policies, including premium increases or the imposition of large deductible or co-insurance requirements, could adversely affect our reputation, business, financial condition and results of operations.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, and anti-corruption and anti-money laundering laws and regulations, including the Foreign Corrupt Practices Act ("FCPA"), the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, clinical research organizations, contractors and other collaborators and partners from authorizing, promising, offering, providing, soliciting or receiving, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties for clinical trials outside of the United States, to sell our products internationally once we enter a commercialization phase, and/or to obtain necessary permits, licenses, patent registrations and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, clinical research organizations, contractors and other collaborators and partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

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

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

We are an emerging growth company and a smaller reporting company, and the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors.

We are an emerging growth company, as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company until December 31, 2024, although circumstances could cause us to lose that status earlier, including if we become a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act or if we have total annual gross revenue of \$1.07 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31 or, if we issue more than \$1.0 billion in non-convertible debt during any three year period before that time, we would cease to be an emerging growth company immediately. Even after we no longer

qualify as an emerging growth company, we may still qualify as a “smaller reporting company” which would allow us to take advantage of many of the same exemptions from disclosure requirements including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. Investors may find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. As a result, changes in rules of accounting principles generally accepted in the United States of America or their interpretation, the adoption of new guidance or the application of existing guidance to changes in our business could significantly affect our financial position and results of operations.

We are also a “smaller reporting company” as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as our voting and non-voting common stock held by non-affiliates is less than \$250.0 million measured on the last business day of our second fiscal quarter, or our annual revenue is less than \$100.0 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is less than \$700.0 million measured on the last business day of our second fiscal quarter.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act and the rules and regulations of Nasdaq. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal controls over financial reporting. Each fiscal year, we must perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our Form 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. This will require that we incur substantial additional professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts. Prior to our initial public offering, we have never been required to test our internal controls within a specified period, and, as a result, we may experience difficulty in meeting these reporting requirements in a timely manner.

We may discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our consolidated financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system’s objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities.

We have incurred and will continue to incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. We are subject to the reporting requirements of the Exchange

Act, which require, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and Nasdaq to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as “say on pay” and proxy access. Recent legislation permits emerging growth companies to implement many of these requirements over a longer period. We intend to take advantage of this new legislation, but we may be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect the rules and regulations applicable to public companies to continue to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will decrease our net income or increase our consolidated net loss and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

If securities or industry analysts publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

We lease 11,200 square feet of space for our headquarters in Foster City, California under an agreement that expires in March 2025. We also lease approximately 1,400 square feet of space for an office in Basel, Switzerland under an agreement that expires in May 2024. We believe that our existing facilities are adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms.

Item 3. Legal Proceedings.

From time to time, we may become involved in legal proceedings relating to claims arising from the ordinary course of business. Our management believes that there are currently no claims or actions pending against us, the ultimate disposition of which could have a material adverse effect on our results of operations, financial condition or cash flows.

Item 4. Mine Safety Disclosures.

None.

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

Our common stock has been listed on the Nasdaq Global Market under the symbol "MIRM" since July 18, 2019. Prior to that date, there was no public market for our common stock.

Holders of Common Stock

As of March 5, 2021, there were 30,419,707 shares of our common stock outstanding held by approximately 15 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

Securities Authorized for Issuance Under Equity Compensation Plans

See Item 12 of Part III of this Annual Report for information about our equity compensation plans which is incorporated by reference herein.

Stock Performance Graph

Not applicable.

Use of Proceeds

We commenced our initial public offering ("IPO") pursuant to the registration statement on Form S-1 (File No. 333-232251) that was declared effective on July 17, 2019 and registered an aggregate of 5,750,000 shares of our common stock. On July 17, 2019, we sold 5,000,000 shares of our common stock at a public offering price of \$15.00 per share for aggregate gross proceeds of \$75.0 million. In July 2019, we completed our IPO. Citigroup Global Markets Inc., Evercore Group L.L.C. and Guggenheim Securities LLC served as joint book-running managers. Raymond James & Associates, Inc. served as lead manager. Roth Capital Partners, LLC served as co-manager.

The underwriting discounts and commissions for our IPO totaled approximately \$5.3 million. We incurred additional costs of approximately \$2.5 million in offering expenses, which when added to the underwriting discounts and commissions paid by us, amounts to total fees and costs of approximately \$7.8 million. Thus, net offering proceeds to us, after deducting underwriting discounts, commissions and offering expenses, were \$67.2 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates.

Upon receipt, the net proceeds from our IPO were held in cash and cash equivalents and investments. Through December 31, 2020, we have used approximately \$19.0 million of the net proceeds from our IPO. We are investing these funds in a combination of short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government. We expect to use the net proceeds from our IPO as described under "Use of Proceeds" in our prospectus dated July 17, 2019 that forms a part of our Registration Statement on Form S-1 (File No. 333-232251), as filed with the SEC pursuant to Rule 424(b) under the Securities Act on July 18, 2019. We cannot predict with certainty all of the particular uses for the

net proceeds from our IPO, or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual use of the net proceeds will vary depending on numerous factors, including our ability to access additional financing, the relative success and cost of our clinical trials. As a result, our management will have broad discretion in the application of the net proceeds, and investors will be relying on our judgment regarding the application of the net proceeds from our IPO.

Item 6. Selected Financial Data.

Not applicable.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes included in Item 8 “Financial Statements and Supplementary Data” and included elsewhere in this Annual Report. This discussion and analysis contains forward-looking statements based upon our current beliefs, estimates, plans and expectations that involve risks, uncertainties and assumptions. Our actual results may differ materially from those contained in these forward-looking statements as a result of various factors, including those set forth under “Risk Factors” or in other parts of this Annual Report.

Overview

We are a biopharmaceutical company focused on the development and commercialization of a late-stage pipeline of novel therapies for debilitating liver diseases. We focus on diseases for which the unmet medical need is high and the biology for treatment is clear. Our pipeline consists of two clinical-stage product candidates with mechanisms of action that have potential utility across a wide range of orphan cholestatic liver diseases. We are developing maralixibat for the treatment of pediatric patients with Alagille syndrome (“ALGS”), progressive familial intrahepatic cholestasis (“PFIC”) and biliary atresia (“BA”). In the third quarter of 2020, we initiated a rolling submission of a New Drug Application (“NDA”), for the treatment of cholestatic pruritus in patients with ALGS to the U.S. Food and Drug Administration (“FDA”) and subsequently completed our NDA submission in January 2021. We are planning for a potential launch in ALGS in the second half of 2021. We have also submitted a marketing authorization application (“MAA”) to the European Medicines Agency (“EMA”) for maralixibat for the treatment of PFIC2, which has been accepted for review. In parallel, we are also conducting the Phase 3 MARCH clinical trial in PFIC evaluating higher doses of maralixibat in a broader population of PFIC subtypes, for which we expect to complete enrollment in the second quarter of 2021 and announce topline data in early 2022. Additionally, we have initiated recruitment for the EMBARK Phase 2 clinical trial for BA. We are developing volixibat for the treatment of adult patients with cholestatic liver diseases, including primary sclerosing cholangitis (“PSC”), intrahepatic cholestasis of pregnancy (“ICP”) and primary biliary cholangitis (“PBC”). We dosed the first patient in the VISTAS Phase 2b clinical trial of volixibat in PSC in January 2021, and we have initiated recruitment for the OHANA clinical trial of ICP. We expect to dose the first patient in the clinical trial of volixibat in PBC in the second half of 2021.

We were incorporated in May 2018 and commenced operations in November 2018. To date, we have focused primarily on acquiring and in-licensing our product candidates, maralixibat and volixibat, organizing and staffing our company, business planning, raising capital, advancing our product candidates through clinical development and preparing for commercialization of maralixibat.

We have a limited operating history and incurred significant operating losses since our inception and expect to continue to incur significant operating losses for the foreseeable future. We have no products approved for commercial sale and have never generated any revenues from product sales. We have funded our operations to date primarily through debt and equity financings.

Financing Transactions

In July 2019, we completed our initial public offering (“IPO”) pursuant to which we sold an aggregate of 5,000,000 shares of our common stock at a price of \$15.00 per share, resulting in net proceeds of \$67.2 million after deducting underwriting discounts, commissions and offering expenses payable by us. Upon the closing of our IPO, all outstanding shares of our Series A convertible preferred stock automatically converted into 14,969,118 shares of our common stock.

In January 2020, we completed a follow-on public offering of our common stock pursuant to which we sold an aggregate of 2,400,000 shares of common stock at a price of \$20.00 per share, resulting in net proceeds of \$44.7 million after deducting underwriting discounts, commissions and offering expenses payable by us.

In August 2020, the Securities and Exchange Commission (“SEC”) declared effective a registration statement on Form S-3 (“Shelf Registration”) covering the sale of up to \$300.0 million of our securities. Also, in August 2020, we entered into a sales agreement (“Sales Agreement”) with SVB Leerink LLC (“SVB Leerink”) pursuant to

which we may elect to issue and sell, from time to time, shares of common stock having an aggregate offering price of up to \$75.0 million under the Shelf Registration through SVB Leerink acting as the sales agent and/or principal. During the year ended December 31, 2020, we sold 305,969 shares of common stock in at-the-market offerings pursuant to the Sales Agreement at a weighted-average price of \$21.55 per share, resulting in gross proceeds of \$6.6 million. The net proceeds after deducting sales commissions to SVB Leerink and other issuance expenses were approximately \$6.3 million. The remaining capacity under the Sales Agreement is approximately \$68.4 million as of December 31, 2020.

In December 2020, we completed an underwritten public offering of our common stock pursuant to the Shelf Registration. We sold 3,750,000 shares of common stock at a price of \$20.00 per share, resulting in net proceeds of \$70.0 million after deducting underwriting discounts, commissions and offering expenses. In addition, we granted the underwriters an option, exercisable for 30 days, to purchase up to 562,500 additional shares of our common stock at the public offering price, less the underwriting discounts and commissions. In January 2021, the underwriters exercised their option for 375,654 shares of our common stock, resulting in net proceeds of \$7.1 million after deducting underwriting discounts.

In December 2020, we entered into a Revenue Interest Purchase Agreement (“RIPA”) with Mulholland SA LLC, an affiliate of Oberland Capital LLC (“Oberland”), as agent for purchasers party thereto (the “Purchasers”), and the Purchasers named therein, pursuant to which the Purchasers paid us \$50.0 million on closing, less certain issuance costs. We may also be entitled to receive up to an additional \$100.0 million upon certain regulatory approval of our product candidates and up to an additional \$50.0 million at the option of the Purchasers to finance in-license or other acquisitions (“Purchaser Payments”). As consideration for the Purchaser Payments, the Purchasers have the right to receive certain revenue interests (the “Revenue Interests”) from us based on the net sales of maralixibat, if approved, which will be tiered payments ranging from 2.00% to 9.75% of our net sales in the covered territory. The initial Revenue Interest rate of 9.75% will decrease upon certain revenue achievements. The Purchasers’ rights to receive such payments shall terminate on the date on which the Purchasers have received payments totaling 195.0% of the total payments made by the Purchasers to the Company, exclusive of transaction expenses, unless the RIPA is terminated earlier. Refer to Note 6 to our audited financial statements included elsewhere in this Annual Report on Form 10-K.

Concurrently with our entry into the RIPA, we entered into a Common Stock Purchase Agreement (the “Stock Purchase Agreement”) with TPC Investments II LP, TPC Investments Solutions LP and TPC Investments Solutions Co-Invest LP, each of which is an affiliate of Oberland. Pursuant to the Stock Purchase Agreement, we issued an aggregate of 509,164 shares of our common stock at a price per share of \$19.64, resulting in net proceeds to us of \$10.0 million.

Financial Overview

Our net loss was \$103.3 million and \$52.6 million for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had an accumulated deficit of \$173.2 million and cash, cash equivalents and investments of \$231.8 million.

We expect our expenses and operating losses will increase substantially as we conduct our ongoing and planned clinical trials, continue our research and development activities, continue commercial preparation activities for maralixibat, and seek regulatory approvals for our product candidates, as well as hire additional personnel and protect our intellectual property. In addition, as our product candidates progress through development and toward commercialization, we will need to make milestone payments to the licensors and other third parties from whom we have in-licensed or acquired our product candidates. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending in particular on the timing of our clinical trials and non-clinical studies and our expenditures on other research and development activities.

We do not expect to generate any revenue from product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our product candidates, which could take a number of years. If we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution.

Accordingly, until such time as we can generate substantial product revenues to support our cost structure, if ever, we expect to finance our cash needs through equity offerings, debt financings or other capital sources, including through the RIPA, collaborations, licenses and other similar arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies. If we are unable to raise additional capital when needed, we could be forced to delay, limit, reduce or terminate the development of one or more of our product candidates or future commercialization efforts or grant rights to develop and market our product candidates even if we would otherwise prefer to develop and market such product candidates ourselves.

COVID-19

The COVID-19 pandemic has had a significant economic impact across the global marketplace presenting challenges to maintaining business continuity. We are working diligently to ensure the advancement of all of our clinical development programs in the safest manner possible. While we are unable to reliably estimate the duration or extent of any potential business disruption or financial impact during this time, we remain committed to (i) prioritizing the safety, health and well-being of patients, their caregivers, healthcare providers and our employees; (ii) ensuring patients are well supported and have continued uninterrupted access to our product candidates, for which we currently do not expect any supply disruption; and (iii) advancing our clinical trials. Examples include a “Work from Home Policy” for our employees and access to home health care to assist families with safer participation in our trials.

Although we did not see a significant financial impact to our business operations as a result of COVID-19 for the year ended December 31, 2020, there may be potential impacts to our business in the future that are highly uncertain and difficult to predict such as temporary closures of our offices or those of our third-party manufacturers or suppliers, disruptions or restrictions on our employees’ ability to travel, disruptions to or delays in ongoing non-clinical trials, clinical trials, third-party manufacturing supply and other operations, the potential diversion of healthcare resources away from the conduct of clinical trials to focus on pandemic concerns, interruptions or delays in the operations of the FDA or other regulatory authorities, and our ability to raise capital and conduct business development activities.

We continue to believe that existing cash, cash equivalents and investments and existing sources of and access to financing are adequate to satisfy our needs for working capital, capital expenditures, debt service requirements and other business development initiatives that we plan to strategically pursue. However, should the COVID-19 pandemic and any associated recession or depression continue for a prolonged period, our results of operations, financial condition, liquidity and cash flows could be materially impacted as a result of a lower likelihood of effectively and efficiently developing new medicines and successfully commercializing our products.

Assignment and License Agreement with Shire (Takeda)

In November 2018, we entered into an assignment and license agreement (“Shire License Agreement”) with Shire International GmbH (“Shire”), which was subsequently acquired by Takeda Pharmaceutical Company Limited, in which we were granted an exclusive, royalty bearing worldwide license to develop and commercialize our two product candidates, maralixibat and volixibat. As part of the Shire License Agreement, we were assigned license agreements held by Shire with Satiogen Pharmaceuticals, Inc. (“Satiogen” and altogether, the “Satiogen License”), Pfizer Inc. (“Pfizer”), and Sanofi-Aventis Deutschland GmbH (“Sanofi”), collectively the Assigned License Agreements (“Assigned License Agreements”). In partial consideration for the rights granted to us under the Shire License Agreement, we made an upfront payment to Shire of \$7.5 million and issued Shire 1,859,151 shares of our common stock with an estimated fair value of \$7.0 million.

Under the Shire License Agreement and Assigned License Agreements, we have paid aggregate development milestones of \$3.0 million in July 2019 related to initiation of the Phase 3 MARCH clinical trial of maralixibat in PFIC, \$10.0 million in December 2020 upon acceptance of an MAA filing to the EMA for maralixibat for the treatment of PFIC2 and \$2.0 million in January 2021 associated with the initiation of the VISTAS Phase 2b clinical trial of volixibat in PSC. Development milestones achieved prior to regulatory approval of the product are expensed in the period incurred as research and development.

See Note 7 to our consolidated financial statements included elsewhere in this Annual Report.

Components of Results of Operations

Operating Expenses

Research and Development Expenses

Research and development expenses primarily relate to clinical development and manufacturing activities of our product candidates. Our research and development expenses include or could include:

- salaries and related expenses for employee personnel, including benefits, travel and expenses related to stock-based compensation granted to personnel in development functions;
- external expenses paid to clinical trial sites, contract research organizations and consultants that conduct our clinical trials;
- expenses related to drug formulation development and the production of clinical trial supplies, including fees paid to contract manufacturers;
- licensing milestone payments related to development or regulatory events;
- expenses related to non-clinical studies;
- expenses related to compliance with drug development regulatory requirements; and
- other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation of equipment, and other supplies.

We expense research and development costs as incurred. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are delivered or the services are performed.

Because our product candidates are still in clinical development and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of product candidates or whether, or when, we may achieve profitability. However, as we add additional development programs, our research and development expenses will increase. We do not track costs on a project-by-project basis. As our programs advance, we intend to track the external and internal cost of each program.

General and Administrative Expense

General and administrative expenses consist primarily of salaries and employee-related costs, including stock-based compensation, for personnel in executive, finance and other administrative functions. Other significant costs include facility-related costs, legal fees relating to intellectual property and corporate matters, professional fees for accounting and consulting services and insurance costs.

We expect that our general and administrative expenses will increase as we expand our operating activities, including commercial preparation activities and increased headcount.

Interest Income

Interest income consists of interest earned on our cash equivalents and investments.

Interest Expense

Interest expense for the year ended December 31, 2020 was related to the RIPA. Costs during the year consist primarily of costs associated with our credit facility and non-cash interest costs associated with the amortization of the related debt discount and deferred issuance costs.

Other Expense, Net

Other expense, net consists of transactional currency exchange loss.

Critical Accounting Policies and Estimates

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

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report, we believe the following accounting policies are the most critical for fully understanding and evaluating our financial condition and results of operations.

Revenue Interest Liability

In December 2020, we entered into the RIPA to support the commercialization and further development of maralixibat and provide for other working capital needs. We recorded a revenue interest liability related to the RIPA on our consolidated balance sheet on the date we entered into the RIPA, which is presented net of issuance costs and a debt discount. We impute interest expense associated with this liability using the effective interest rate method. The estimated effective interest rate is calculated based on the rate that would enable the debt to be repaid in full over the anticipated life of the arrangement. Interest expense and amortization of our issuance costs and debt discount is recognized over the estimated term in our consolidated statements of operations. The interest rate on the liability may vary during the term of the agreement primarily due to the level of forecasted net sales. We evaluate the interest rate quarterly based on our current net sales forecasts utilizing the prospective method. A significant increase or decrease in net sales could materially impact the revenue interest liability, interest expense and the time period for repayment.

At December 31, 2020, the revenue interest liability is calculated using our current estimate of global forecasted net sales of maralixibat for our planned commercial launch and impacted by a debt discount comprising the estimated value of a bifurcated derivative liability and issuance costs incurred. As our product candidates are not yet approved for sale, the estimated probability and timing or amounts of repayment is likely to change each reporting period.

The fair value of the derivative liability is valued using a "with-and-without" method. The "with-and-without" methodology involves valuing the whole instrument on an as-is basis and then valuing the instrument without the individual embedded derivative. The difference between the entire instrument with the embedded derivative compared to the instrument without the embedded derivative was the fair value of the derivative liability. The estimated probability and timing of underlying events triggering the exercisability of the derivative liability bifurcated from within the RIPA, forecasted cash flows and the discount rate are significant unobservable inputs used to determine the estimated fair value of the entire instrument with the embedded derivative.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our 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 when we have not yet been invoiced or otherwise notified of the actual cost. We accrue and expense clinical trial activities performed by third parties based upon estimates of the proportion of work completed over the life of the individual study and patient enrollment rates in accordance with agreements established with clinical research organizations, clinical trial sites and other vendors associated with the clinical trials. We determine the estimates by reviewing contracts, vendor agreements and purchase orders and through discussions with internal clinical personnel and external service providers as to the progress or stage of completion of trials or services and the agreed-upon fee to be paid for such services.

We make estimates of accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments, if necessary. If the actual timing of the performance of services or the level of effort varies from the estimate, we will adjust the accrual accordingly. Nonrefundable advance payments for goods and services, including fees for process development or manufacturing and distribution of clinical supplies that will be used in future research and development activities, are deferred and recognized as expense in the period that the related goods are consumed or services are performed.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Stock-Based Compensation

We recognize compensation costs related to stock-based awards granted to employees and directors, including stock options, based on the estimated fair value of the awards on the date of grant. We estimate the grant date fair value, and the resulting stock-based compensation, using the Black-Scholes option-pricing model. The grant date fair value of the stock-based awards is generally recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards.

The Black-Scholes option-pricing model requires the use of subjective assumptions to determine the fair value of stock-based awards. These assumptions include:

- *Fair value of common stock*—For grants prior to our IPO in July 2019, the fair value of our common stock underlying share-based awards was estimated on each grant date by our board of directors. In order to determine the fair value of our common stock underlying option grants, our board of directors considered, among other things, valuations of our common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accountants Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. For all grants subsequent to our IPO in July 2019, the fair value of common stock is determined by using the closing price per share of common stock as reported on the Nasdaq Global Market.
- *Expected term*— The expected term represents the period that stock-based awards are expected to be outstanding. The expected term for option grants is determined using the simplified method. The simplified method deems the term to be the average of the time-to-vesting and the contractual life of the stock-based awards.
- *Expected volatility*— We use an average historical stock price volatility of comparable public companies within the biotechnology and pharmaceutical industry that were deemed to be representative of future stock price trends as we do not have sufficient trading history for our common stock. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.
- *Risk-free interest rate*—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.
- *Expected dividend*—We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

The assumptions used in our Black-Scholes option-pricing model represent management's best estimates at the time of measurement. These estimates are complex, involve a number of variables, uncertainties and assumptions and the application of management's judgment, as they are inherently subjective. If any assumptions change, our stock-based compensation could be materially different in the future.

For the years ended December 31, 2020 and 2019, stock-based compensation was \$12.6 million and \$6.1 million, respectively. As of December 31, 2020, we had \$33.3 million of total unrecognized stock-based compensation which we expect to recognize over a weighted-average period of 2.7 years.

Recent Accounting Pronouncements

A description of recent accounting pronouncements that may potentially impact our financial position, results of operations or cash flows is disclosed in Note 2 to our consolidated financial statements included elsewhere in this Annual Report.

Results of Operations for the Years Ended December 31, 2020 and 2019

The following table summarizes our results of operations for the years ended December 31, 2020 and 2019 (in thousands):

	Year Ended December 31,		Change
	2020	2019	
Operating expenses:			
Research and development	\$ 81,605	\$ 42,991	\$ 38,614
General and administrative	22,691	11,752	10,939
Total operating expenses	104,296	54,743	49,553
Loss from operations	(104,296)	(54,743)	(49,553)
Other income (expense):			
Interest income	1,559	2,232	(673)
Interest expense	(335)	—	(335)
Other expense, net	(192)	(21)	(171)
Net loss before provision for income taxes	(103,264)	(52,532)	(50,732)
Provision for income taxes	6	21	(15)
Net Loss	\$ (103,270)	\$ (52,553)	\$ (50,717)

Research and Development Expenses

Research and development expenses were \$81.6 million for the year ended December 31, 2020, an increase of \$38.6 million compared to the year ended December 31, 2019. The increase was primarily due to \$12.3 million related to manufacturing activities supporting NDA registration activities and clinical supply chain, \$10.2 million of personnel and other compensation related expenses, including an increase in stock-based compensation of \$2.8 million, reflecting an increase in the number of development employees to support the increase in our clinical trials and development activities, \$10.0 million of development milestone expense incurred upon acceptance of an MAA filing to the EMA for maralixibat for the treatment of PFIC2, \$6.6 million of clinical trial expenses consisting of approximately \$5.0 million for newly initiated volixibat clinical trials in PSC and ICP and \$1.6 million for maralixibat primarily related to BA, \$2.8 million of consulting expenses associated with our increased clinical, manufacturing and regulatory activities, and \$0.9 million associated with quality assurance systems and resources in connection with regulatory filings. These increases were partially offset by a decrease of \$3.0 million associated with development milestone expense related to the initiation of the Phase 3 MARCH clinical trial incurred during 2019, \$1.1 million for clinical trial expenses related to natural history studies associated with PFIC and a decrease of \$0.4 million for expenses related to transition services provided by Shire in 2019.

General and Administrative Expenses

General and administrative expenses were \$22.7 million for the year ended December 31, 2020, an increase of \$10.9 million compared to the year ended December 31, 2019. The increase was primarily due to \$6.5 million of personnel and other compensation related expenses including an increase in stock-based compensation of \$3.7 million, reflecting an increase in our number of administrative employees to support increased requirements of operating as a public company, such as regulatory requirements and compliance, and commercial preparation activities for maralixibat, \$2.1 million of expenses associated with operating as a public company primarily related to increased costs of insurance and audit and tax fees, \$1.7 million of professional and consulting services primarily associated with commercial preparation activities for maralixibat, and \$0.6 million of expenses related to other general and administrative expenses.

Interest Income

Interest income was \$1.6 million for the year ended December 31, 2020, a decrease of \$0.7 million compared to the year ended December 31, 2019. The decrease was primarily due to lower interest earned on our cash equivalents and investment balances compared to the prior year largely a result of current economic conditions.

Interest Expense

Interest expense was \$0.3 million for the year ended December 31, 2020 compared to zero for the year ended December 31, 2019. The increase was related to the accreted interest on the revenue interest liability in connection with the RIPA.

Liquidity and Capital Resources

Overview

We had \$231.8 million of cash, cash equivalents and investments as of December 31, 2020 compared to \$140.0 million as of December 31, 2019. Since inception, we have incurred operating losses and negative cash flows from operations. As of December 31, 2020, we had an accumulated deficit of \$173.2 million.

In July 2019, we completed our IPO, pursuant to which we sold an aggregate of 5,000,000 shares of our common stock at a price of \$15.00 per share, resulting in net proceeds of \$67.2 million after deducting underwriting discounts, commissions and offering expenses payable by us.

In January 2020, we completed a follow-on public offering of our common stock pursuant to which we sold an aggregate of 2,400,000 shares of common stock at a price of \$20.00 per share, resulting in net proceeds of \$44.7 million after deducting underwriting discounts, commissions and offering expenses payable by us.

In August 2020, SEC declared effective the Shelf Registration covering the sale of up to \$300.0 million of our securities. Also, in August 2020, we entered into the Sales Agreement with SVB Leerink, pursuant to which we may elect to issue and sell, from time to time, shares of common stock having an aggregate offering price of up to \$75.0 million under the Shelf Registration through SVB Leerink acting as the sales agent and/or principal. During the year ended December 31, 2020, we sold 305,969 shares of common stock in an at-the-market offering pursuant to the Sales Agreement at a weighted-average price of \$21.55 per share, resulting in gross proceeds of \$6.6 million. The net proceeds after deducting sales commissions to SVB Leerink and other issuance expenses were approximately \$6.3 million. The remaining capacity under the Sales Agreement is approximately \$68.4 million as of December 31, 2020.

In December 2020, we completed an underwritten public offering of our common stock pursuant to the Shelf Registration. We sold 3,750,000 shares of common stock at a price of \$20.00 per share, resulting in net proceeds of \$70.0 million after deducting underwriting discounts, commissions and offering expenses. In addition, we granted the underwriters an option, exercisable for 30 days, to purchase up to 562,500 additional shares of our common stock at the public offering price, less the underwriting discounts and commissions. In January 2021, the underwriters exercised their option for 375,654 shares of our common stock resulting in net proceeds of \$7.1 million after deducting underwriting discounts.

Pursuant to the RIPA, we received a net upfront cash payment of \$49.3 million after deducting issuance costs, and may be entitled to receive up to an additional \$100.0 million upon certain regulatory events related to our product candidates and up to an additional \$50.0 million at the option of the Purchasers to finance in-license or other acquisitions. In return, the Purchasers will have a right to receive Revenue Interests based on net sales of maralexibat, if approved. As of December 31, 2020, we have not generated any revenue from product sales, and we anticipate that we will continue to incur losses for the foreseeable future.

Pursuant to the Stock Purchase Agreement, entered into concurrently with our entry into the RIPA, we issued an aggregate of 509,164 shares of our common stock at a price per share of \$19.64, resulting in net proceeds to us of \$10.0 million.

Based on our current and anticipated level of operations, we believe our cash, cash equivalents and investments will be sufficient to fund current operations through at least the next 12 months. Our cash, cash equivalents and investments include money market funds, government agency securities, corporate debt and commercial paper. We maintain established guidelines relating to diversification and maturities of our investments to preserve principal and maintain liquidity.

We anticipate that we will continue to incur net losses for the foreseeable future as we continue research efforts and the development of our product candidates, continue commercial preparation activities for maralixibat, hire additional staff, including clinical, scientific, operational, financial and management personnel and pay potential development and commercial milestones in connection with our license agreements.

Our primary use of cash is to fund operating expenses, which consist primarily of research and development expenditures, and to a lesser extent, general and administrative expenditures, including commercial planning expenses. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

Until such time, if ever, as we can generate substantial product revenue from sales of maralixibat, volixibat or any future product candidates, we expect to finance our cash needs through a combination of equity offerings, debt financings, revenue interest purchase agreements and potential collaboration, license or development agreements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect rights as a stockholder. Debt financing and preferred equity 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 or declaring dividends.

If we raise additional funds through the RIPA, collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. As a result of the COVID-19 pandemic and actions taken to slow its spread, the global credit and financial markets have experienced volatility and disruptions, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. If the equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. 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 drug development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We have based our projections of operating capital requirements on assumptions that may prove to be incorrect and we may use all our available capital resources, which consist of cash, cash equivalents and investments, sooner than we expect. Because of the numerous risks and uncertainties associated with research, development and commercialization of our products, we are unable to estimate the exact amount of our operating capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- the cost of commercialization activities if our product candidates or any future product candidates are approved or cleared for sale, including marketing, sales and distribution costs;
- the cost of establishing sales and marketing activities;
- the number and characteristics of any future product candidates we develop or acquire;
- the timing of any cash milestone payments pursuant to the Shire License Agreement as well as our other license and acquisition agreements if we successfully achieve certain predetermined milestones;
- our ability to forecast demand for our products, scale our supply to meet that demand and manage working capital effectively
- the cost of manufacturing our product or any future product candidates and any products we successfully commercialize, including costs associated with building our supply chain;

- our ability to establish and maintain strategic collaborations, the RIPA, licensing or other arrangements and the financial terms of any such agreements that we may enter into;
- any product liability or other lawsuits related to our products;
- the expenses needed to attract and retain skilled personnel;
- the costs associated with being a public company;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs related to maralixibat and volixibat, and the outcome of this and any other future patent litigation we may be involved in; and
- the timing, receipt and amount of sales of any future approved or cleared products, if any.

Cash Flows

The following table provides a summary of the net cash flow activity for the periods indicated (in thousands):

	<u>Year Ended December 31,</u>	
	<u>2020</u>	<u>2019</u>
Net cash used in operating activities	\$ (89,075)	\$ (39,362)
Net cash provided by (used in) investing activities	37,874	(127,781)
Net cash provided by financing activities	181,288	127,177
Effect of exchange rate on cash and cash equivalents	29	(27)
Net increase (decrease) in cash and cash equivalents	<u>\$ 130,116</u>	<u>\$ (39,993)</u>

Cash Used in Operating Activities

Net cash used in operating activities was \$89.1 million for the year ended December 31, 2020, reflecting our net loss of \$103.3 million partially offset by non-cash items of \$13.6 million. Non-cash items consisted primarily of \$12.6 million of stock-based compensation, \$0.6 million of depreciation and amortization of our fixed assets and our operating lease right-of use assets and \$0.3 million of interest expense in connection with the RIPA. Additionally, cash used in operating activities reflected changes in net operating assets of \$0.6 million, consisting primarily of a \$3.7 million increase in accounts payable, accrued expenses and other liabilities due to clinical and manufacturing activities, offset by a \$1.8 million increase to prepaid expenses primarily associated with clinical and manufacturing activities, \$1.0 million increase in long term assets primarily associated with advances to vendors associated with our clinical trials, and a \$0.4 million decrease in our operating lease liability.

Net cash used in operating activities was \$39.4 million for the year ended December 31, 2019, reflecting our net loss of \$52.6 million partially offset by non-cash items of \$6.1 million. Non-cash items consisted primarily of \$6.1 million in stock-based compensation, \$0.3 million in depreciation and amortization of our operating lease right-of-use assets and fixed assets and \$0.3 million of discount accretion on our investments. Additionally, cash used in operating activities reflected changes in net operating assets of \$7.1 million, consisting primarily of an \$10.1 million increase in accounts payable, accrued expenses and other liabilities primarily due to clinical and manufacturing activities, a \$2.7 million increase in prepaid expenses and other current assets consisting primarily of \$1.4 million in prepayments for directors and officers insurance, \$0.8 million in prepaid research and development expenses representing increased operating activities over 2018 and \$0.4 million in interest receivable, and a \$0.2 million increase in other assets.

Cash Used in Investing Activities

Net cash provided by investing activities was \$37.9 million for the year ended December 31, 2020 primarily due to proceeds of \$85.9 million from maturities of investments and proceeds of \$26.8 million from paydowns of investments, partially offset by \$74.6 million used in purchases of investments and \$0.2 million used for purchases of property and equipment.

Net cash used in investing activities was \$127.8 million for the year ended December 31, 2019 due to the purchases of \$152.0 million of investments and the purchases of \$0.3 million of property and equipment, partially offset by proceeds from maturities of investments of \$24.5 million.

Cash Provided by Financing Activities

Net cash provided by financing activities was \$181.3 million for the year ended December 31, 2020, due to net proceeds of \$44.7 million received from the completion of a follow-on public offering of our common stock pursuant to which we sold an aggregate of 2,400,000 shares of common stock at a price of \$20.00 per share, net proceeds of \$70.0 million received from completion of a public offering of our common stock pursuant to which we sold an aggregate of 3,750,000 shares of common stock at \$20.00 per share, net proceeds of \$49.6 million pursuant to the RIPA, net proceeds of \$10.0 million pursuant to the Stock Purchase Agreement entered into in connection with the RIPA for the sale of an aggregate of 509,164 shares of our common stock at a price per share of \$19.64, net proceeds of \$6.3 million from the sale of common stock under the Sales Agreement with SVB Leerink, pursuant to which we sold an aggregate of 305,969 shares of common stock at a weighted-average price of \$21.55 per share, and proceeds of \$0.8 million from the issuance of common stock pursuant to the exercise of outstanding options pursuant to our equity incentive plans. These proceeds were offset by the payment of \$0.2 million for deferred offering costs associated with the Shelf Registration. The deferred offering costs are reflected as other assets on our consolidated balance sheet until such time as we complete sales of shares under the Shelf Registration.

Net cash provided by financing activities was \$127.2 million for the year ended December 31, 2019, primarily due to \$67.2 million in net proceeds received from our IPO and \$60.0 million in net proceeds from the issuance of 59,844,699 shares of Series A convertible preferred stock.

Contractual Obligations

The following table summarizes our principal contractual obligations and commitments as of December 31, 2020 that will affect our future liability (in thousands):

	Payments due by period				
	Total	Less than 1 year	1 – 3 Years	3 – 5 Years	More than 5 years
Operating lease obligations(1)	\$ 3,844	\$ 869	\$ 2,745	\$ 230	\$ —

(1) Consists of leases for our corporate headquarters encompassing approximately 11,200 square feet of office space that expires in March 2025, and the lease for our office space in Basel, Switzerland encompassing approximately 1,400 square feet that expires in May 2024.

The above table does not include our obligations under the RIPA as products are not yet approved for sale and the timing or amounts of repayment is likely to change each reporting period. Refer to Note 6 to our audited financial statements included elsewhere in this Annual Report on Form 10-K for further information.

From time to time we enter into certain types of contracts that contingently require us to indemnify parties against third-party claims, including the Shire License Agreement, RIPA, and certain real estate leases, supply purchase agreements, and agreements with directors and officers. The terms of such obligations vary by contract and in most instances a maximum dollar amount is not explicitly stated therein. Generally, amounts under these contracts cannot be reasonably estimated until a specific claim is asserted, thus no liabilities have been recorded for these obligations on our consolidated balance sheet for the periods presented.

We enter into contracts in the normal course of business with clinical research organizations and clinical sites for the conduct of clinical trials, non-clinical research studies, professional consultants for expert advice and other vendors for clinical supply manufacturing or other services. These contracts generally provide for termination on notice, and therefore are cancelable contracts.

Contractual Arrangements

Under the Shire License Agreement, as well as our other license and acquisition agreements, we have payment obligations that are contingent upon future events such as our achievement of specified development, regulatory and commercial milestones and are required to make royalty payments in connection with the sale of products developed under those agreements. Under the Shire License Agreement and Assigned License Agreements, we have paid development milestones of \$3.0 million in July 2019 related to initiation of the Phase 3 MARCH clinical trial, \$10.0 million in December 2020 upon acceptance of an MAA filing to the EMA for maralixibat for the treatment of PFIC2 and \$2.0 million in January 2021 associated with the initiation of the VISTAS Phase 2b clinical trial of volixibat in PSC. As of December 31, 2020, we were unable to estimate the timing or likelihood of achieving the remaining future milestones or making future product sales and, therefore, any related payments are not included herein. For additional information regarding these license agreements, including our payment obligations thereunder, see Note 7 to our consolidated financial statements included elsewhere in this Annual Report.

JOBS Act

As an emerging growth company under the Jumpstart Our Business Startups Act of 2012 (“JOBS Act”), we can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. We intend to rely on other exemptions provided by the JOBS Act, including without limitation, not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act of 2002 (“Sarbanes-Oxley Act”).

We will remain an emerging growth company until the earliest of (i) December 31, 2024, (ii) the last day of the fiscal year in which we have total annual gross revenue of at least \$1.07 billion, (iii) the last day of the fiscal year in which we are deemed to be a “large accelerated filer” as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended (“Exchange Act”), or (iv) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk.

Interest Rate Risk

Our cash, cash equivalents and investments as of December 31, 2020 consist of readily available checking, money market funds, and investments. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. However, because of the short-term nature of the instruments in our portfolio, a sudden change in market interest rates would not be expected to have a material impact on our financial condition and/or results of operations. We do not believe that our cash, cash equivalents or investments have significant risk of default or illiquidity. While we believe our cash, cash equivalents and investments do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash and cash equivalents at one financial institution that is in excess of federally insured limits.

We have entered into the RIPA. Our primary exposure to market risk is that the interest rate on the liability may vary during the term of the agreement primarily due to the level of forecasted net sales. A significant increase or decrease in net sales will materially impact the revenue interest liability, interest expense and the time period for repayment. We do not believe a change in interest rate has had a material effect on our results of operations during the year ended December 31, 2020.

Foreign Currency Rate Risk

Our operations include activities in the United States and Switzerland. In addition, we contract with vendors that are located outside of the United States and certain invoices are denominated in foreign currencies. While our operating results are exposed to changes in foreign currency exchange rates between the U.S. dollar and various foreign currencies, the most significant of which are the Swiss Franc and the Euro, we do not currently believe that foreign currency could have a significant impact.

Effects of Inflation

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation and changing prices had a significant impact on our results of operations for any periods presented herein.

Item 8. Financial Statements and Supplementary Data.

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Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Mirum Pharmaceuticals, Inc. (the Company) as of December 31, 2020 and 2019, the related consolidated statements of operations, comprehensive loss, redeemable convertible preferred stock, redeemable common stock and stockholders' equity (deficit) and cash flows for each of the two years in the period ended December 31, 2020, 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, 2020 and 2019, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2020, 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.

/s/ Ernst & Young LLP

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

Irvine, California
March 9, 2021

Mirum Pharmaceuticals, Inc.
Consolidated Balance Sheets
(In thousands, except share and per share data)

	December 31,	
	2020	2019
Assets		
Current assets:		
Cash and cash equivalents	\$ 142,086	\$ 11,970
Short-term investments	89,734	104,690
Prepaid expenses and other current assets	4,530	2,703
Total current assets	236,350	119,363
Long-term investments	—	23,292
Property and equipment, net	1,293	1,372
Operating lease right-of-use assets	1,949	2,361
Other assets	1,272	324
Total assets	<u>\$ 240,864</u>	<u>\$ 146,712</u>
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	\$ 3,151	\$ 3,351
Accrued expenses	13,411	9,328
Operating lease liabilities	636	397
Derivative liability	1,264	—
Total current liabilities	18,462	13,076
Revenue interest liability, net	47,651	—
Operating lease liabilities, noncurrent	2,627	3,251
Other liabilities	29	36
Total liabilities	68,769	16,363
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, \$0.0001 par value; 10,000,000 shares authorized as of December 31, 2020 and 2019, respectively; zero shares issued and outstanding as of December 31, 2020 and 2019, respectively; and liquidation value of \$0 as of December 31, 2020 and 2019, respectively	—	—
Common stock, \$0.0001 par value; 200,000,000 shares authorized as of December 31, 2020 and 2019, respectively; 30,032,600 shares issued and 29,776,544 shares outstanding, excluding 256,056 shares subject to repurchase as of December 31, 2020; and 22,989,987 shares issued and 22,600,338 shares outstanding, excluding 389,649 shares subject to repurchase as of December 31, 2019	3	2
Additional paid-in capital	345,180	200,119
Accumulated deficit	(173,171)	(69,901)
Accumulated other comprehensive income	83	129
Total stockholders' equity	172,095	130,349
Total liabilities and stockholders' equity	<u>\$ 240,864</u>	<u>\$ 146,712</u>

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

Mirum Pharmaceuticals, Inc.
Consolidated Statements of Operations
(In thousands, except share and per share data)

	Year Ended December 31,	
	2020	2019
Operating expenses:		
Research and development	\$ 81,605	\$ 42,991
General and administrative	22,691	11,752
Total operating expenses	104,296	54,743
Loss from operations	(104,296)	(54,743)
Other income (expense):		
Interest income	1,559	2,232
Interest expense	(335)	—
Other expense, net	(192)	(21)
Net loss before provision for income taxes	(103,264)	(52,532)
Provision for income taxes	6	21
Net loss	\$ (103,270)	\$ (52,553)
Net loss per share, basic and diluted	\$ (4.09)	\$ (4.58)
Weighted-average shares of common stock outstanding, basic and diluted	25,251,968	11,486,367

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

Mirum Pharmaceuticals, Inc.
Consolidated Statements of Comprehensive Loss
(In thousands)

	Year Ended December 31,	
	2020	2019
Net loss	\$ (103,270)	\$ (52,553)
Other comprehensive gain (loss):		
Unrealized (loss) gain on available-for-sale investments	(75)	156
Cumulative translation adjustments	29	(27)
Comprehensive loss	<u>\$ (103,316)</u>	<u>\$ (52,424)</u>

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

Mirum Pharmaceuticals, Inc.
Consolidated Statements of Redeemable Convertible Preferred Stock,
Redeemable Common Stock and Stockholders' Equity (Deficit)
(In thousands, except share and per share data)

	Series A Redeemable Convertible Preferred Stock		Redeemable Common Stock		Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
Balance as of December 31, 2018	59,908,284	\$ 59,849	1,859,151	\$ 6,990	—	\$ —	636,719	\$ 1	\$ 34	\$ (17,348)	\$ —	\$ (17,313)
Issuance of Series A redeemable convertible preferred stock at \$1.00259507 per share, net of issuance costs of \$23	59,844,699	59,977	—	—	—	—	—	—	—	—	—	—
Issuance of common stock in initial public offering, net of issuance costs of \$7,800	—	—	—	—	—	—	5,000,000	—	67,200	—	—	67,200
Conversion of Series A redeemable convertible preferred stock into common stock on initial public offering	(119,752,983)	(119,826)	—	—	—	—	14,969,118	1	119,825	—	—	119,826
Reclassification of redeemable common stock into common stock on initial public offering	—	—	(1,859,151)	(6,990)	—	—	1,859,151	—	6,990	—	—	6,990
Restricted common stock vested in the period	—	—	—	—	—	—	135,350	—	—	—	—	—
Stock-based compensation	—	—	—	—	—	—	—	—	6,070	—	—	6,070
Net loss	—	—	—	—	—	—	—	—	—	(52,553)	—	(52,553)
Other comprehensive income	—	—	—	—	—	—	—	—	—	—	129	129
Balance as of December 31, 2019	—	\$ —	—	\$ —	—	\$ —	22,600,338	\$ 2	\$ 200,119	\$ (69,901)	\$ 129	\$ 130,349
Issuance of common stock in underwritten public offerings, net of issuance costs of \$8,322	—	—	—	—	—	—	6,150,000	1	114,678	—	—	114,679
Issuance of common stock in connection with Revenue Interest Purchase Agreement	—	—	—	—	—	—	509,164	—	10,766	—	—	10,766
Issuance of common stock in at-the-market offerings, net of issuance costs of \$314	—	—	—	—	—	—	305,969	—	6,279	—	—	6,279
Issuance of common stock in connection with common stock option exercises	—	—	—	—	—	—	47,604	—	328	—	—	328
Issuance of common stock in connection with Employee Stock Purchase Plan	—	—	—	—	—	—	29,876	—	456	—	—	456
Restricted common stock vested in the period	—	—	—	—	—	—	133,593	—	—	—	—	—
Stock-based compensation	—	—	—	—	—	—	—	—	12,554	—	—	12,554
Net loss	—	—	—	—	—	—	—	—	—	(103,270)	—	(103,270)
Other comprehensive loss	—	—	—	—	—	—	—	—	—	—	(46)	(46)
Balance as of December 31, 2020	—	\$ —	—	\$ —	—	\$ —	29,776,544	\$ 3	\$ 345,180	\$ (173,171)	\$ 83	\$ 172,095

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

Mirum Pharmaceuticals, Inc.
Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,	
	2020	2019
Operating activities		
Net loss	\$ (103,270)	\$
Reconciliation of net loss to net cash used in operating activities:		
Stock-based compensation	12,554	
Depreciation and amortization	305	
Amortization of operating lease right-of-use assets	318	
Non-cash interest expense related to the revenue interest liability	335	
Net amortization (accretion) on investments	72	
Change in operating assets and liabilities:		
Prepaid and other current assets	(1,827)	
Operating lease right-of-use assets	94	
Other assets	(954)	
Accounts payable, accrued expenses and other liabilities	3,683	
Operating lease liabilities	(385)	
Net cash used in operating activities	(89,075)	
Investing activities		
Proceeds from maturities of investments	85,900	
Proceeds from paydown of investments	26,761	
Purchase of investments	(74,562)	
Purchase of property and equipment	(225)	
Net cash provided by (used in) investing activities	37,874	
Financing activities		
Proceeds from the issuance of Series A redeemable convertible preferred stock, net of issuance costs	—	
Proceeds from issuance of common stock in public offerings, net of issuance costs	121,087	
Proceeds from issuance of common stock in private placement, net of issuance costs	10,000	
Proceeds from issuance of common stock pursuant to equity award plans	784	
Proceeds from revenue interest liability, net of issuance costs	49,575	
Payment of deferred offering costs in connection with the shelf registration and sales agreement	(158)	
Net cash provided by financing activities	181,288	
Effect of exchange rate on cash and cash equivalents	29	
Net increase (decrease) in cash and cash equivalents	130,116	
Cash and cash equivalents at beginning of period	11,970	
Cash and cash equivalents at end of period	\$ 142,086	\$
Supplemental disclosure of cash flow information:		
Cash paid for income taxes	\$ 11	\$
Operating cash flows paid for operating lease	\$ 576	\$
Noncash investing and financing activities:		
Revenue interest liability issuance costs included in accrued liabilities	\$ 229	\$
Deferred offering costs included in accrued liabilities	\$ 129	\$
Compound derivative liability related to revenue interest liability	\$ 1,264	\$
Operating lease right-of-use asset obtained in exchange for operating lease liability	\$ —	\$
Landlord paid tenant improvements	\$ —	\$
Conversion of Series A redeemable convertible preferred stock into common stock on initial public offering	\$ —	\$
Reclassification of redeemable common stock into common stock on initial public offering	\$ —	\$

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

Mirum Pharmaceuticals, Inc.
Notes to Consolidated Financial Statements

1. Organization and Description of Business

Mirum Pharmaceuticals, Inc. (the “Company”) was incorporated in the State of Delaware on May 2, 2018, and is headquartered in Foster City, California. The Company is a biopharmaceutical company focused on the development and commercialization of a late-stage pipeline of novel therapies for debilitating liver diseases. The Company’s pipeline consists of two clinical-stage product candidates, maralixibat and volixibat, with mechanisms of action that have potential utility across a wide range of orphan liver diseases. The Company commenced significant operations in November 2018.

The consolidated financial statements include the accounts of the Company and its wholly owned subsidiary, Mirum Pharmaceuticals AG. All intercompany balances and transactions among the consolidated entities have been eliminated in consolidation.

The Company views its operations and manages its business as one operating segment.

Reverse Stock Split

In July 2019, the Company effected a 1-for-8 reverse stock split of its common stock. The par value and the authorized number of shares of common stock were not adjusted as a result of the reverse stock split. The reverse stock split resulted in an adjustment to the conversion price of the Company’s Series A redeemable convertible preferred stock (the “Series A Preferred Stock”) to reflect a proportional decrease in the number of shares of common stock to be issued upon conversion. The accompanying consolidated financial statements and notes to the consolidated financial statements give retroactive effect to the reverse stock split for all periods presented.

Liquidity

The Company has a limited operating history, has incurred significant operating losses since its inception, and the revenue and income potential of the Company’s business and market are unproven. As of December 31, 2020, the Company had an accumulated deficit of \$173.2 million and cash, cash equivalents and investments of \$231.8 million, which are available to fund future operations. The Company believes that its cash, cash equivalents and investments as of December 31, 2020 provide sufficient capital resources to continue its operations for at least twelve months from the issuance date of the accompanying consolidated financial statements. The consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business. The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of this uncertainty. Management expects to continue to incur additional substantial losses in the foreseeable future as a result of the Company’s research and development activities.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (“GAAP”).

Use of Estimates

The preparation of consolidated financial statements in accordance with GAAP requires management to make estimates and assumptions that impact the reported amounts of assets, liabilities and expenses and the disclosure of contingent assets and liabilities in the financial statements and accompanying notes. The most significant estimates in the Company’s consolidated financial statements relate to the revenue interest liability, accrued research and development expenses, the valuation of derivative liabilities and the valuation allowance of deferred tax assets resulting from net operating losses. These estimates and assumptions are based upon historical experience,

knowledge of current events and various other factors believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities and the recording of expenses that are not readily apparent from other sources. Actual results could differ materially from those estimates.

In December 2019, a novel strain of coronavirus, which causes COVID-19, was identified. Due to the rapid and global spread of the virus, on March 11, 2020, the World Health Organization declared the COVID-19 outbreak a pandemic. To slow the proliferation of COVID-19, governments have implemented extraordinary measures, which include the mandatory closure of businesses, restrictions on travel and gatherings, and quarantine and physical distancing requirements.

There were no significant estimates contained in the preparation of the Company's consolidated financial statements or impacts to the Company's consolidated financial statements for the year ended December 31, 2020 that were directly a result of the COVID-19 pandemic. The Company is not aware of any specific event or circumstance that would require an update to its estimates, judgments and assumptions or a revision of the carrying value of the Company's assets or liabilities as of the date of this filing.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less at the date of purchase to be cash equivalents. The carrying amounts reported in the consolidated balance sheets for cash and cash equivalents are valued at cost, which approximate their fair value. Cash equivalents may consist of money market accounts, money market funds, U.S. treasury bills and repurchase agreements.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash and cash equivalents, and short and long-term investments. The Company minimizes the amount of credit exposure by investing cash that is not required for immediate operating needs in money market funds, government obligations and/or commercial paper with short maturities. To date, the Company has not experienced any losses associated with this credit risk and continues to believe that this exposure is not significant.

Investments

The Company classifies all investments as available-for-sale, as the sale of such securities may be required prior to maturity. Management determines the appropriate classification of its investments in debt securities at the time of purchase. Investments with original maturities beyond three months at the date of purchase and which mature at, or less than twelve months from the balance sheet date, are classified as a current asset.

Investments are recorded at fair value, with unrealized gains and losses reported as accumulated other comprehensive income (loss) until realized. The Company periodically evaluates whether declines in fair values of its available-for-sale securities below their book value are other-than-temporary. This evaluation consists of several qualitative and quantitative factors regarding the severity and duration of the unrealized loss as well as the Company's ability and intent to hold the available-for-sale security until a forecasted recovery occurs. Additionally, the Company assesses whether it has plans to sell the security or it is more likely than not it will be required to sell any available-for-sale securities before recovery of its amortized cost basis. The cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion, as well as interest and dividends, are included in interest income. Realized gains and losses from the sale of available-for-sale securities, if any, are determined on a specific identification basis and are also included in interest income. To date, the Company has not identified any other than temporary declines in fair value of its investments.

Fair Value of Financial Instruments

The accounting guidance defines fair value, establishes a consistent framework for measuring fair value and expands disclosure for each major asset and liability category measured at fair value on either a recurring or nonrecurring basis. Fair value is defined as an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in

pricing an asset or liability. As a basis for considering such assumptions, the accounting guidance establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

Level 1: Observable inputs such as quoted prices in active markets;

Level 2: Inputs, other than the quoted prices in active markets, that are observable either directly or indirectly; and

Level 3: Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions.

The carrying amounts of all cash equivalents, accounts payable and accrued liabilities are reasonable estimates of their fair value.

Property and Equipment

Property and equipment are recorded at cost less accumulated depreciation. Depreciation is computed on a straight-line basis over the estimated useful lives of the related assets, ranging from three to five years. Leasehold improvements are amortized over the shorter of their useful lives or the related lease term. As of December 31, 2020, property and equipment consisted primarily of leasehold improvements of \$1.3 million and furniture and equipment of \$0.3 million. As of December 31, 2019, property and equipment consisted primarily of leasehold improvements of \$1.3 million and furniture and equipment of \$0.2 million. Accumulated depreciation as of December 31, 2020 and 2019 was \$0.3 million and \$0.1 million, respectively.

Impairment of Long-Lived Assets

Long-lived assets are reviewed for indications of possible impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparison of the carrying amounts to the future undiscounted cash flows attributable to these assets. An impairment loss is recognized to the extent an asset group is not recoverable, and the carrying amount exceeds the projected discounted future cash flows arising from these assets. There were no impairments of long-lived assets for any of the periods presented.

Deferred Offering Costs

Deferred offering costs directly related to the Company's shelf registration and sales agreement primarily consisted of legal, accounting, printing and SEC filing fees. These costs are reclassified to additional paid-in capital on a pro-rata basis as the Company completes offerings under the shelf registration, with any remaining deferred costs to be charged to results of operations at the end of the three-year life of the shelf registration. During the year ended December 31, 2020, the deferred offering costs reclassified to additional paid-in capital as a result of the transactions contemplated under a shelf registration were \$59,000.

Accrued Research and Development Expenses

The Company accrues and expenses clinical trial activities performed by third parties based upon estimates of the proportion of work completed over the life of the individual study and patient enrollment rates in accordance with agreements established with clinical research organizations and clinical trial sites. The Company determines the estimates by reviewing contracts, vendor agreements and purchase orders and through discussions with internal clinical personnel and external service providers as to the progress or stage of completion of trials or services and the agreed-upon fee to be paid for such services.

The Company makes estimates of accrued expenses as of each balance sheet date based on facts and circumstances known to the Company at that time. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company will adjust the accrual accordingly. The Company has not experienced any material differences between accrued costs and actual costs incurred for the periods presented. Nonrefundable advance payments for goods and services are deferred and recognized as expense in the period that the related goods are consumed or services are performed.

Revenue Interest Liability, Net

The revenue interest liability, net, associated with the Revenue Interest Purchase Agreement (“RIPA”) that the Company entered into in December 2020 with Mulholland SA LLC, an affiliate of Oberland Capital LLC (“Oberland”), as agent for purchasers party thereto (the “Purchasers”), and the Purchasers, is presented net of issuance costs and a debt discount on the consolidated balance sheets. The Company imputes interest expense associated with this liability using the effective interest rate method. The effective interest rate is calculated based on the rate that would enable the debt to be repaid in full over the anticipated life of the arrangement. The interest rate on the liability may vary during the term of the agreement depending on a number of factors, including the level of forecasted net sales. The Company evaluates the interest rate quarterly based on its current net sales forecasts utilizing the prospective method. A significant increase or decrease in net sales will materially impact the revenue interest liability, interest expense and the time period for repayment.

Derivative Liability

The RIPA contains certain features that meet the definition of being embedded derivatives requiring bifurcation as a separate compound financial instrument apart from the RIPA. The derivative liability is initially measured at fair value on issuance and is subject to remeasurement at each reporting period with changes in fair value recognized as other income (expense) in the consolidated statements of operations as the change in fair value of derivative liability.

Research and Development Expenses

Research and development expenses consist primarily of fees paid to contract research organizations and other vendors for clinical, non-clinical and manufacturing services, salaries and benefits, including stock-based compensation, consultant expenses, costs related to acquiring manufacturing materials, costs related to compliance with regulatory requirements and license payments related to acquiring intellectual property rights for the Company’s product candidates. Research and development expenses are expensed as incurred.

Leases

The Company determines if a contractual arrangement is or contains a lease at inception. Operating lease right-of-use (“ROU”) assets represent the Company’s right to use an underlying asset during the lease term, and operating lease liabilities represent the Company’s obligation to make lease payments arising from the lease. Operating leases are included in ROU assets, current operating lease liabilities, and long-term operating lease liabilities on the accompanying consolidated balance sheets. Operating lease ROU assets and lease liabilities are initially recognized based on the present value of the future minimum lease payments over the lease term at commencement date calculated using the Company’s incremental borrowing rate applicable to the lease asset, unless the implicit rate is readily determinable. Operating lease ROU assets also include any lease payments made at or before lease commencement and exclude any lease incentives received. The Company determines the lease term as the noncancelable period of the lease and may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. Leases with a term of 12 months or less are not recognized on the consolidated balance sheet. The Company’s leases do not contain any residual value guarantees. Lease expense for minimum lease payments is recognized as rent expense on a straight-line basis over the lease term. Variable lease payments include lease operating expenses.

Stock-Based Compensation

The Company recognizes stock-based compensation for all stock-based awards to employees based on the grant-date fair value of the award. The Company estimates the fair value of stock option grants using the Black-Scholes option pricing model, and the assumptions used in calculating the fair value of stock-based awards represent management’s estimates and involve inherent uncertainties and the application of management’s judgment. The fair value of equity awards that are expected to vest is amortized on a straight-line basis over the requisite service period. Stock-based compensation is recognized net of actual forfeitures when they occur. All stock-based compensation costs are recorded in the consolidated statements of operations and comprehensive loss based upon the underlying employee’s role within the Company.

Income Taxes

Income taxes are recorded using the liability method, under which deferred tax assets and liabilities are determined based on differences between financial reporting and tax basis of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. Valuation allowances are recorded against deferred tax assets when it is determined it is more-likely-than-not that some or all of the tax benefits will not be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of Financial Accounting Standards Board (“FASB”) Accounting Standards Codification No. 740, *Income Taxes* (“ASC 740”). When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit would more likely than not be realized assuming examination by the taxing authority. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances.

Interest and penalties related to unrecognized tax benefits, if any, are recorded as a component of income tax expense.

Net Loss Per Share

Basic net loss per share is computed by dividing net loss attributable to common stockholders by the weighted-average shares of common stock outstanding for the period, without consideration for potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted-average shares of common stock and potentially dilutive securities outstanding for the period determined using the treasury-stock and if-converted methods. Diluted net loss per share excludes the potential impact of the Company’s common stock subject to repurchase, common stock options, contingently issuable employee stock purchase plan shares and contingently issuable overallotment shares because their effect would be anti-dilutive due to the Company’s net loss. Since the Company incurred a net loss in each of the periods presented, basic and diluted net loss per share were the same.

The following outstanding potentially dilutive shares have been excluded from the calculation of diluted net loss per share for the periods presented due to their anti-dilutive effect:

	December 31,	
	2020	2019
Options to purchase common stock	5,071,740	3,366,812
Common stock subject to repurchase	256,056	389,649
Employee stock purchase plan contingently issuable	12,931	—
Overallotment shares contingently issuable	562,500	—
Total	5,903,227	3,756,461

Recently Adopted Accounting Pronouncements

On January 1, 2020, the Company adopted Accounting Standards Update (“ASU”) No. 2018-13, *Disclosure Framework — Changes to the Disclosure Requirements for Fair Value Measurement (Topic 820)*, which eliminated the requirements to disclose the amount and reasons for transfers between Level 1 and Level 2 assets, the policy for timing and transfers between levels and the valuation process for Level 3 fair value measurements. The guidance modified disclosure requirements for investments in certain entities that calculate net asset value and clarifies the purpose of the measurement uncertainty disclosure. The guidance added requirements to disclose changes in unrealized gains or losses included in other comprehensive income for recurring Level 3 fair value measurements and to disclose the range and weighted average used to develop significant unobservable inputs for Level 3 fair value measurements. There was no impact on the accompanying consolidated financial statements as of the adoption date, January 1, 2020.

In December 2019, the FASB issued ASU No. 2019-12, *Simplifying the Accounting for Income Taxes (Topic 740)*. The guidance eliminates certain exceptions for recognizing deferred taxes for investments, performing intraperiod allocation and calculating income taxes in interim periods. This guidance also includes guidance to

reduce complexity in certain areas, including recognizing deferred taxes for tax goodwill and allocating taxes to members of a consolidated group. ASU 2019-12 is effective for annual and interim periods in fiscal years beginning after December 15, 2020. Early adoption is permitted. The Company early adopted this guidance in the fourth quarter of 2020. The adoption did not have a material impact on the Company's consolidated financial statements.

Other recent accounting pronouncements issued by the FASB (including its Emerging Issues Task Force), the American Institute of Certified Public Accountants, and the Securities and Exchange Commission ("SEC") did not, or are not believed by management to, have a material impact on the Company's consolidated financial position, results of operations or cash flows.

Recent Accounting Pronouncements Not Yet Adopted

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"). ASU 2016-13 requires an entity to utilize a new impairment model that requires measurement and recognition of expected credit losses for most financial assets and certain other instruments, including but not limited to available-for-sale debt securities. Credit losses relating to available-for-sale debt securities will be recorded through an allowance for credit losses rather than as a direct write-down to the security. The new guidance requires the use of forward-looking expected credit loss models based on historical experience, current conditions, and reasonable and supportable forecasts that affect the collectability of the reported amount, which may result in earlier recognition of credit losses under the new guidance. The new guidance also modifies the impairment models for available-for-sale debt securities and for purchased financial assets with credit deterioration since their origination. Subsequent to the issuance of ASU 2016-13, the FASB issued ASU 2018-19, *Codification Improvements to Topic 326, Financial Instruments - Credit Losses*. This ASU does not change the core principle of the guidance in ASU 2016-13, instead these amendments are intended to clarify and improve operability of certain topics included within the credit losses guidance. The FASB also subsequently issued ASU No. 2019-04, *Codification Improvements to Topic 326, Financial Instruments—Credit Losses, Derivatives and Hedging (Topic 815), and Financial Instruments (Topic 842)*, which did not change the core principle of the guidance in ASU 2016-13 but clarified that expected recoveries of amounts previously written off and expected to be written off should be included in the valuation account and should not exceed amounts previously written off and expected to be written off. In March 2020, the FASB issued ASU No. 2020-3, *Codification Improvements to Financial Instruments* which makes narrow-scope improvements to various financial instruments topics, including the new credit losses standard and clarifies the following areas (i) the contractual term of a net investment in a lease should be the contractual term used to measure expected credit losses; (ii) when an entity regains control of financial assets sold, an allowance for credit losses should be recorded. The guidance is effective for fiscal years, and interim periods within those years, beginning after December 15, 2019 for public business entities, excluding smaller reporting companies. For smaller reporting companies, the guidance will be effective during the first quarter of 2023. The Company is in the process of assessing the impact adoption will have on its consolidated financial statements.

In August 2020, the FASB issued ASU No. 2020-06, *Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging-Contracts in Entity's Own Equity (Subtopic 815-40)* ("ASU 2020-06"), which simplifies the accounting for convertible instruments. The guidance removes certain accounting models that separate the embedded conversion features from the host contract for convertible instruments. ASU 2020-06 allows for a modified or full retrospective method of transition. This update is effective for fiscal years beginning after December 15, 2021, and interim periods within those fiscal years. Early adoption is permitted. The Company is currently evaluating the impact this change will have on its consolidated financial statements.

3. Fair Value Measurements

Financial assets and liabilities subject to fair value measurements on a recurring basis and the level of inputs used in such measurements by major security type are presented in the following table (in thousands):

	December 31, 2020			
	Level 1	Level 2	Level 3	Total
Financial assets:				
Money market fund	\$ 127,783	\$ —	\$ —	\$ 127,783
U.S. treasury bills	29,997	—	—	29,997
Corporate debt securities	—	23,201	—	23,201
Commercial paper	—	41,460	—	41,460
U.S. government bonds	—	5,066	—	5,066
Asset-backed securities	—	2,006	—	2,006
Total financial assets	\$ 157,780	\$ 71,733	\$ —	\$ 229,513
Financial liabilities:				
Derivative liability	—	—	1,264	1,264
Total financial liabilities	\$ —	\$ —	\$ 1,264	\$ 1,264

	December 31, 2019			
	Level 1	Level 2	Level 3	Total
Financial assets:				
Money market fund	\$ 10,621	\$ —	\$ —	\$ 10,621
Corporate debt securities	—	41,668	—	41,668
Commercial paper	—	35,016	—	35,016
U.S. government bonds	—	22,511	—	22,511
Asset-backed securities	—	28,787	—	28,787
Total	\$ 10,621	\$ 127,982	\$ —	\$ 138,603

The carrying amounts of certain financial instruments such as cash and cash equivalents, prepaid expenses, other current assets, accounts payable, accrued expenses, and other current liabilities as of December 31, 2020 and December 31, 2019 approximate their related fair values due to the short-term maturities of these instruments. Certain financial instruments classified within Level 2 of the fair value hierarchy include the types of instruments that trade in markets that are not considered to be active, but are valued based on quoted market prices, broker or dealer quotations, or alternative pricing sources with reasonable levels of price transparency. The carrying amount of the revenue interest liability as of December 31, 2020 approximates its fair value and is based on the Company's contractual repayment obligation to the Purchasers, based on the current estimates of future revenues, over the life of the RIPA. The liability is considered a Level 3 input based on the three-level hierarchy. Refer to Note 6 "Revenue Interest Purchase Agreement" for further information.

Derivative Liability

The debt pursuant to the RIPA contains embedded derivatives requiring bifurcation as a single compound derivative instrument. The Company estimated the fair value of the derivative liability on issuance and at December 31, 2020 using a "with-and-without" method. The "with-and-without" methodology involves valuing the whole instrument on an as-is basis and then valuing the instrument without the individual embedded derivative. The difference between the entire instrument with the embedded derivative compared to the instrument without the embedded derivative was the fair value of the derivative liability on issuance and at December 31, 2020. The estimated probability and timing of underlying events triggering the exercisability of the put options contained within the RIPA, forecasted cash flows and the discount rate are significant unobservable inputs used to determine the estimated fair value of the entire instrument with the embedded derivative. As of the inception date and December 31, 2020, the discount rate used for valuation to the derivative liability is 15.9%.

The following table provides a summary of the change in the estimated fair value of the Company's derivative liability, classified as Level 3 in the fair value hierarchy:

Balance at January 1, 2020	\$	—
Initial fair value of derivative liability		1,264
Balance at December 31, 2020	\$	<u>1,264</u>

4. Financial Instruments

The fair value and amortized cost of cash equivalents and available-for-sale investments by major security type are presented in the following table (in thousands):

	December 31, 2020			Estimated Fair Value
	Amortized Cost	Unrealized Gain	Unrealized Loss	
Cash equivalents and investments:				
Money market fund	\$ 127,783	—	—	\$ 127,783
U.S. treasury bills	29,995	2	—	29,997
Corporate debt securities	23,126	75	—	23,201
Commercial paper	41,460	—	—	41,460
U.S. government bonds	5,067	—	(1)	5,066
Asset-backed securities	2,001	5	—	2,006
Total cash equivalents and investments	<u>\$ 229,432</u>	<u>\$ 82</u>	<u>\$ (1)</u>	<u>\$ 229,513</u>
Classified as:				
Cash equivalents				\$ 139,779
Short-term investments				89,734
Total cash equivalents and investments				<u>\$ 229,513</u>

	December 31, 2019			Estimated Fair Value
	Amortized Cost	Unrealized Gain	Unrealized Loss	
Cash equivalents and investments:				
Money market fund	\$ 10,621	\$ —	\$ —	\$ 10,621
Corporate debt securities	41,556	113	(1)	41,668
Commercial paper	35,016	—	—	35,016
U.S. government bonds	22,492	19	—	22,511
Asset-backed securities	28,762	25	—	28,787
Total cash equivalents and investments	<u>\$ 138,447</u>	<u>\$ 157</u>	<u>\$ (1)</u>	<u>\$ 138,603</u>
Classified as:				
Cash equivalents				\$ 10,621
Short-term investments				104,690
Long-term investments				23,292
Total cash equivalents and investments				<u>\$ 138,603</u>

As of December 31, 2020, the remaining contractual maturities of available-for-sale debt securities were less than 12 months. During the years ended December 31, 2020 and 2019, there have been no significant realized gains or losses on available-for-sale investments. During the years ended December 31, 2020 and 2019, no investments had been in a continuous unrealized loss position for more than 12 months and the Company did not recognize any other-than-temporary impairment losses on these securities.

5. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31,	
	2020	2019
Accrued clinical trials	3,673	4,795
Accrued professional service fees	2,157	777
Accrued contract manufacturing and non-clinical costs	2,780	1,540
Accrued compensation and related benefits	4,801	2,216
Total accrued expenses	<u>\$ 13,411</u>	<u>\$ 9,328</u>

6. Revenue Interest Purchase Agreement

In December 2020, the Company entered into the RIPA to obtain financing for the commercialization and further development of maralixibat and other working capital needs. Pursuant to the RIPA, the Company received \$50.0 million in December 2020, less certain transaction expenses.

The Company may be entitled to receive up to approximately \$150.0 million in subsequent installments as follows: (i) \$65.0 million upon acceptance for review by the U.S. Food and Drug Administration (“FDA”) of a New Drug Application submitted by the Company for maralixibat as a treatment for pruritus due to Alagille syndrome (“ALGS”) on or prior to a specified date; (ii) \$35.0 million upon FDA approval of maralixibat as a treatment for ALGS on or prior to a specified date; and (iii) up to \$50.0 million at the option of the Purchasers to finance in-licenses or other acquisitions on or prior to December 31, 2022.

As consideration for such payments, the Purchasers have the right to receive certain revenue interests (the “Revenue Interests”) from the Company based on annual net sales of maralixibat, if approved, which will be tiered payments (the “Revenue Interest Payments”) based on whether such annual net sales are (i) less than or equal to \$350.0 million (“Tier 1”), (ii) exceeding \$350.0 million and less than or equal to \$1.1 billion (“Tier 2”), or (iii) exceeding \$1.1 billion (“Tier 3”).

The Revenue Interest Payments will initially be 9.75% (at Tier 1) and 2.00% (at Tier 2 and Tier 3) of such annual net sales. If the Purchasers have received Revenue Interest Payments in an amount equal to or greater than 110.0% of the total payments actually made by the Purchasers to the Company, exclusive of transaction expenses (the “Cumulative Purchaser Payments”), on or prior to December 31, 2026, the Revenue Interests shall be reduced to 2.00% at Tier 1 and 0.00% at Tier 3 for all subsequent calendar years beginning on January 1, 2027. If the Purchasers have not received Revenue Interest Payments in an amount equal to or greater than 110.0% of the Cumulative Purchaser Payments on or prior to December 31, 2026, the Revenue Interests shall be increased for all subsequent calendar years beginning on January 1, 2027 to a single defined rate (with no separate tiers) that would have provided the Purchasers with an amount equal to 110.0% of the Cumulative Purchaser Payments on or prior to December 31, 2026 had such rate applied to Tier 1 of initial Revenue Interest Payments. The Purchasers’ rights to receive the Revenue Interest Payments shall terminate on the date on which the Purchasers have received Revenue Interest Payments of 195.0% of the Cumulative Purchaser Payments, unless the RIPA is terminated earlier.

Under the RIPA, the Company has an option (the “Call Option”) to terminate the RIPA and repurchase future Revenue Interests at any time upon advance written notice. Additionally, the Purchasers have an option (the “Put Option”) to terminate the RIPA and to require the Company to repurchase future Revenue Interests upon enumerated events such as a bankruptcy event, an uncured material breach, a material adverse effect or a change of control, or upon the 12th anniversary of the first payment made by Purchasers. If the Put Option is exercised prior to the first anniversary of the closing date by the Purchasers (except pursuant to a change of control), the required repurchase price will be 120.0% of the Cumulative Purchaser Payments (minus all payments Company has made to the Purchasers in connection with the Revenue Interests). In all other cases, if the Put Option or the Call Option are exercised, the required repurchase price will be 175.0% of the Cumulative Purchaser Payments (minus all payments Company has made to the Purchasers in connection with the Revenue Interests), if such option is exercised prior to

the third anniversary of the closing date, and 195.0% of the Cumulative Purchaser Payments (minus all payments Company has made to the Purchasers in connection with the Revenue Interests) if such option is exercised thereafter.

In addition, the RIPA contains various representations and warranties, information rights, non-financial covenants, indemnification obligations and other provisions that are customary for a transaction of this nature. The Purchaser's obligations to fund the scheduled installments are subject to certain customary conditions as set forth in the RIPA.

Concurrently with the RIPA, the Company entered into a Common Stock Purchase Agreement ("CSPA") with certain affiliates of Oberland, pursuant to which the Company sold an aggregate of 509,164 shares of its common stock for an aggregate purchase price of \$10.0 million. The \$50.0 million received pursuant to the RIPA and \$10.0 million received pursuant to the CSPA was allocated between the resulting financial instruments on a relative fair value basis, with \$49.2 million allocated to the debt under the RIPA and \$10.8 million allocated to the common stock issued under the CSPA.

The Put Options under the RIPA that are exercisable by Purchasers upon certain contingent events were determined to be embedded derivatives requiring bifurcation and separately accounted for as a single compound derivative instrument. The Company recorded the initial fair value of the derivative liability of \$1.3 million as a debt discount, which will be amortized to interest expense over the expected term of the debt using the effective interest method.

In connection with the RIPA, as of December 31, 2020, \$47.7 million was recorded as a revenue interest liability on the consolidated balance sheet. The Company imputes interest expense associated with this liability using the effective interest rate method. The effective interest rate is calculated based on the rate that would enable the debt to be repaid in full over the anticipated life of the arrangement. The interest rate on this liability may vary during the term of the agreement depending on a number of factors, including the level of forecasted net sales. The Company evaluates the interest rate quarterly based on its current net sales forecasts utilizing the prospective method. A significant increase or decrease in net sales will materially impact the revenue interest liability, interest expense and the time period for repayment. The Company recorded \$0.3 million in interest expense related to this arrangement for the year ended December 31, 2020.

The Company incurred \$0.7 million of issuance costs in connection with the RIPA, which will be amortized to interest expense over the estimated term of the debt.

Revenue Interest Payments made as a result of the Company's net sales will reduce the revenue interest liability.

The following table summarizes the revenue interest liability activity during the year ended December 31, 2020 (in thousands):

Revenue interest liability at inception	\$	49,234
Interest expense recognized		335
Capitalized issuance costs		(654)
Debt discount from embedded derivatives		(1,264)
Revenue interest liability at December 31, 2020	\$	<u>47,651</u>

7. Asset Acquisitions

Assignment and License Agreement with Shire International GmbH (Takeda)

In November 2018, the Company entered into an Assignment and License Agreement (the "Shire Agreement") with Shire International GmbH ("Shire"), which was subsequently acquired by Takeda Pharmaceutical Company Limited, and made an upfront payment to Shire of \$7.5 million and issued Shire 1,859,151 shares of redeemable common stock with an estimated fair value of \$7.0 million, or \$3.76 per share. Under the terms of the Shire

Agreement, Shire granted the Company an exclusive, royalty bearing worldwide license to develop and commercialize its two product candidates, maralixibat and volixibat. As part of the Shire Agreement, the Company was assigned license agreements held by Shire with Satiogen Pharmaceuticals, Inc. (“Satiogen”), Pfizer Inc. (“Pfizer”) and Sanofi-Aventis Deutschland GmbH (“Sanofi”). The Company has the right to sublicense under the Shire Agreement and additionally has the right to sublicense under the Satiogen, Pfizer and Sanofi licenses subject to the terms of those license agreements.

The Company is obligated to pay Shire up to an aggregate of \$109.5 million upon the achievement of certain clinical development and regulatory milestones for maralixibat in certain indications and an additional \$25.0 million upon regulatory approval of maralixibat for each and every other indication. In addition, the Company is required to pay up to an aggregate of \$30.0 million upon the achievement of certain clinical development and regulatory milestones for volixibat solely for the first indication sought. Upon commercialization, the Company is obligated to pay Shire product sales milestones on total licensed products up to an aggregate of \$30.0 million. The Company is also obligated to pay tiered royalties with rates ranging from low double-digits to mid-teens based upon annual worldwide net sales for all licensed products; however, these royalties are reduced in part by royalties due under the Satiogen and Sanofi licenses, as discussed below, related to maralixibat and volixibat, as applicable. The Company’s royalty obligations will continue on a licensed product-by-licensed product and country-by-country basis until the later to occur of the expiration of the last valid claim in a licensed patent covering the applicable licensed product in such country, expiration of any regulatory exclusivity for the licensed product in a country and ten years after the first commercial sale of a licensed product in such country. The Company paid development milestones of \$2.5 million in July 2019 related to the initiation of the Phase 3 MARCH clinical trial of maralixibat in PFIC and \$10.0 million in December 2020 upon acceptance of an MAA filing to the EMA for maralixibat for the treatment of PFIC2. Development milestones achieved prior to regulatory approval of the product are expensed by the Company in the period incurred as research and development. As of December 31, 2020, no additional milestones have been accrued as there were no other potential milestones yet considered probable. In January 2021, the Company achieved a development milestone pursuant to the Shire License Agreement, which triggered a \$2.0 million payment by the Company to Shire associated with the initiation of the VISTAS Phase 2b clinical trial of volixibat in PSC.

In January 2019, the Company also entered into a Transition Services Agreement (“TSA”) with Shire, which covered services provided by Shire to transfer the research and development activities and the related know-how from Shire to the Company, including continuation of work on any existing clinical trials and manufacturing activities until fully transferred. All transition services were completed and all pass-through costs were settled as of June 30, 2019. As such, for the year ended December 31, 2020, there were no expenses for Shire provided services or pass-through costs recorded. The Company recorded \$0.4 million for services provided by Shire under the TSA for the year ended December 31, 2019. Additionally, the Company recorded a reduction of estimated expenses of \$0.1 million for pass-through costs related to continuation of work on existing clinical trials and manufacturing activities for the year ended December 31, 2019. The reduction of estimated expenses for the year ended December 31, 2019 was related to a final reconciliation of expenses and agreement on final amounts due to Shire.

Satiogen License

Through the Shire Agreement, the Company was assigned a license agreement with Satiogen pursuant to which the Company obtained an exclusive, worldwide license to certain patents and know-how, with the right to sublicense to a third party subject to certain financial considerations. The Company is obligated to pay to Satiogen up to an aggregate of \$10.5 million upon the achievement of certain milestones, of which \$0.5 million was for initiation of certain development activities, \$5.0 million for the completion of regulatory approvals and \$5.0 million for commercialization activities. Additionally, the Company will be required to pay a low single-digit royalty on net sales. The Company’s royalty obligations continue on a licensed product-by-licensed product and country-by-country basis until the expiration of the last valid claim in a licensed patent covering the applicable licensed product in such country. Royalty obligations under the Satiogen license are creditable against the royalty obligations to Shire under the Shire Agreement. In July 2019, the Company achieved a development milestone related to the initiation of the Phase 3 MARCH clinical trial of maralixibat in PFIC and made a \$0.5 million payment to Satiogen, which was expensed by the Company as research and development expense. As of December 31, 2020, no additional milestones had been accrued as there were no other potential milestones yet considered probable.

Pfizer License

Through the Shire Agreement, the Company was assigned a license agreement with Pfizer pursuant to which the Company obtained an exclusive, worldwide license to certain Pfizer know-how with a right to sublicense. Upon commercialization of any product utilizing the licensed product, the Company will be required to pay to Pfizer a low single-digit royalty on net sales of product sold by the Company, its affiliates or sublicensees. The Company's royalty obligations continue on a licensed product-by-licensed product basis until the eighth anniversary of the first commercial sale of such licensed product anywhere in the world.

Sanofi License

Through the Shire Agreement, the Company was assigned a license agreement with Sanofi pursuant to which the Company obtained an exclusive, worldwide license to certain patents and know-how with the right to sublicense to a third party subject to certain financial considerations. The Company is obligated to pay up to an aggregate of \$36.0 million upon the achievement of certain regulatory, commercialization and product sales milestones. Additionally, upon commercialization, the Company is required to pay tiered royalties in the mid to high single-digit range based upon net sales of licensed products sold by the Company and sublicensees in a calendar year, subject to adjustments in certain circumstances. The Company's royalty obligations continue on a licensed product-by-licensed product and country-by-country basis until the later to occur of the expiration of the last valid claim in a licensed patent covering the applicable licensed product in such country and ten years after the first commercial sale of a licensed product in such country. Royalty obligations under the Sanofi license are creditable against the royalty obligations to Shire under the Shire Agreement. As of December 31, 2020, no milestones had been accrued as there were no potential milestones yet considered probable.

8. Leases

In January 2019, the Company entered into an operating lease agreement for office space which consisted of approximately 5,600 square feet (the "initial lease"). The lease term is approximately four years with an option to extend the term for one five-year term, which at the time was not reasonably assured of exercise and therefore, not included in the lease term. The lease contained a tenant improvement allowance of \$0.4 million, which has been recorded as leasehold improvements in the accompanying consolidated balance sheets with a corresponding reduction of the ROU asset at inception of the lease. Rent payments commenced in August 2019.

In November 2019, the Company amended the operating lease agreement (the "amended agreement") to extend the term of the initial lease through March 2025. This extension was accounted for as a lease modification and the Company recorded an increase to the ROU asset and lease liability of \$0.6 million at the time of the amendment.

Additionally, pursuant to the amended agreement, the Company expanded the office space by 5,555 square feet for a five-year term expiring in March 2025 (the "expanded space"). The Company accounted for the expanded space as a separate contract as there were material additional rights of use that were not included in the initial lease. The amended lease contained a tenant improvement allowance of \$0.8 million in connection with the expanded space, which has been recorded as leasehold improvements on the accompanying consolidated balance sheet with a corresponding reduction of the ROU asset at inception of the lease for the expanded space.

The ROU and corresponding lease liabilities were estimated using a weighted-average incremental borrowing rate of 8.0%.

As of December 31, 2020, the Company recorded an aggregate ROU asset of \$1.9 million and an aggregate lease liability of \$3.3 million in the accompanying consolidated balance sheet. The weighted-average remaining lease term is 4.1 years.

As of December 31, 2020, undiscounted future minimum payments under the Company's operating leases are as follows (in thousands):

<u>Year Ended December 31,</u>	<u>Undiscounted Rent Payments</u>
2021	869
2022	893
2023	922
2024	930
2025	230
Thereafter	—
Total undiscounted lease payments	3,844
Less: imputed interest	(581)
Total lease liability	<u>\$ 3,263</u>

Rent expense was \$0.6 million and \$0.3 million for the years ended December 31, 2020 and 2019, respectively. Variable lease payments for lease operating expenses were immaterial for the years ended December 31, 2020 and 2019.

9. Stockholders' Equity (Deficit)

Common Stock

In July 2019, the Company completed its initial public offering ("IPO") of its common stock. In connection with its IPO, the Company issued and sold 5,000,000 shares of its common stock at a price of \$15.00 per share. As a result of the IPO, the Company received \$67.2 million in net proceeds, after deducting underwriting discounts, commissions and offering expenses. At the closing of the IPO, 119,752,983 shares of outstanding Series A Preferred Stock were automatically converted into 14,969,118 shares of common stock, and 1,859,151 shares of redeemable common stock were reclassified into permanent equity due to the expiration of the deemed redemption feature. Following the IPO, there were no shares of Series A Preferred Stock or shares of redeemable common stock outstanding.

In connection with the completion of its IPO, the Company amended and restated its certificate of incorporation to provide for 200,000,000 authorized shares of common stock with a par value of \$0.0001 per share and 10,000,000 authorized shares of preferred stock with a par value of \$0.0001 per share. Each share of common stock is entitled to one voting right. Common stockholders are entitled to dividends when funds are legally available and declared by the Company's board of directors.

In January 2020, the Company completed a follow-on public offering of its common stock, pursuant to which the Company sold 2,400,000 shares of common stock at a price of \$20.00 per share, resulting in net proceeds of \$44.7 million after deducting underwriting discounts, commissions and offering expenses.

In August 2020, the SEC declared effective a registration statement on Form S-3 ("Shelf Registration") covering the sale of up to \$300.0 million of the Company's securities. Also, in August 2020, the Company entered into a sales agreement ("Sales Agreement") with SVB Leerink LLC ("SVB Leerink") pursuant to which the Company may elect to issue and sell, from time to time, shares of common stock having an aggregate offering price of up to \$75.0 million under the Shelf Registration through SVB Leerink acting as the sales agent and/or principal. During the year ended December 31, 2020, the Company sold 305,969 shares of common stock in an at-the-market offering pursuant to the Sales Agreement at a weighted-average price of \$21.55 per share, resulting in gross proceeds of \$6.6 million. The net proceeds after deducting sales commissions to SVB Leerink and other issuance expenses were approximately \$6.3 million. The remaining capacity under the Sales Agreement is approximately \$68.4 million as of December 31, 2020.

In December 2020, the Company completed an underwritten public offering of its common stock pursuant to the Shelf Registration. The Company sold 3,750,000 shares of common stock at a price of \$20.00 per share,

resulting in net proceeds of \$70.0 million after deducting underwriting discounts, commissions and offering expenses. In addition, the Company granted the underwriters an option, exercisable for 30 days, to purchase up to 562,500 additional shares of its common stock at the public offering price, less the underwriting discounts and commissions. In January 2021, the underwriters partially exercised their option and purchased 375,654 shares of the Company's common stock at a price of \$20.00 per share, resulting in net proceeds of \$7.1 million after deducting underwriting discounts.

As of December 31, 2020 and 2019, 256,056 and 389,649 shares of common stock, respectively, were subject to repurchase by the Company. The unvested stock liability related to these shares is immaterial to all periods presented.

Common Stock Reserved for Issuance

Common stock reserved for issuance is as follows:

	December 31,	
	2020	2019
Stock options issued and outstanding	5,071,740	3,366,812
Reserved for future stock awards or option grants	2,009,410	1,112,443
Reserved for employee stock purchase plan	700,023	500,000
Reserved for over-allotment shares	562,500	—
	<u>8,343,673</u>	<u>4,979,255</u>

10. Stock-Based Compensation

Equity Incentive Plans

In November 2018, the Company adopted the 2018 Equity Incentive Plan (the "2018 Plan") which permits the granting of stock awards and incentive and nonstatutory stock options to employees, directors and consultants of the Company.

In July 2019, the Company's board of directors and stockholders approved and adopted the 2019 Equity Incentive Plan (the "2019 Plan"). The 2019 Plan became effective on July 17, 2019. Under the 2019 Plan, the Company may grant stock options, stock appreciation rights, restricted stock, restricted stock units and other stock or cash-based awards to individuals who are then employees, officers, directors or consultants of the Company. A total of 1,401,443 shares of common stock were approved to be initially reserved for issuance under the 2019 Plan, including 101,443 shares that remained available for issuance under the 2018 Plan as of July 17, 2019. Shares subject to outstanding awards under the 2018 Plan as of the effective date of the 2019 Plan that are subsequently canceled, forfeited or repurchased by the Company will be added to the shares reserved under the 2019 Plan. In addition, the number of shares of common stock available for issuance under the 2019 Plan will be automatically increased on the first day of each calendar year during the ten-year term of the 2019 Plan, beginning with January 1, 2020 and ending with January 1, 2029, by an amount equal to 5% of the outstanding number of shares of the Company's common stock on December 31st of the preceding calendar year or such lesser amount as determined by the Company's board of directors. As of December 31, 2020, 1,093,210 shares of common stock were available for issuance under the 2019 Plan.

In March 2020, the compensation committee of the Company's board of directors approved and adopted the 2020 Inducement Plan (the "2020 Inducement Plan"). Under the 2020 Inducement Plan, the Company may grant nonstatutory stock options, stock appreciation rights, restricted stock and restricted stock units to new employees entering into employment with the Company in accordance with Nasdaq Listing Rule 5635(c)(4). At adoption, the 2020 Inducement Plan authorized 750,000 shares of the Company's common stock for future issuance. In December 2020, the Company's board of directors authorized an additional 750,000 shares of the Company's common stock for future issuance. As of December 31, 2020, 916,200 shares of common stock were available for issuance under the 2020 Inducement Plan.

Stock Options

The fair value of each employee and non-employee stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. Due to the Company's limited operating history and a lack of company specific historical and implied volatility data, the Company estimated expected volatility based on the historical volatility of a group of similar companies that are publicly traded. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. Due to the lack of historical exercise history, the expected term of the Company's stock options for employees has been determined utilizing the "simplified" method for awards. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is zero based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

The following assumptions were used to estimate the fair value of stock option awards granted during the following period:

	Year ended December 31,	
	2020	2019
Exercise price	\$10.40-\$26.59	\$2.94-\$15.00
Expected term (in years)	5.5-6.1	5.5-6.3
Expected volatility	77.07%-95.85%	73.88%-84.59%
Risk-free interest rate	0.33%-1.73%	1.41%-2.46%
Expected dividend yield	—	—
Grant date fair value of options granted	\$7.38-\$20.21	\$5.10-\$10.46

The following table summarizes stock option activity during the year ended December 31, 2020 (in thousands, except share and per share data):

	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (in Years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2019	3,366,812	\$ 5.14	9.3	\$ 65,235
Granted	2,070,267	\$ 17.87		
Exercised	(47,604)	\$ 6.90		
Canceled and forfeited	(317,735)	\$ 10.45		
Outstanding as of December 31, 2020	5,071,740	\$ 9.99	8.6	\$ 40,631
Vested and exercisable as of December 31, 2020	1,468,291	\$ 5.12	8.1	\$ 18,289

Intrinsic value is calculated as the difference between the exercise price of the underlying options and the fair value of the common stock for the options that had exercise prices that were lower than the per share fair value of the common stock on the date of exercise. The weighted-average grant-date fair value per share of stock options granted during the years ended December 31, 2020 and 2019 was \$12.70 and \$8.29 per share, respectively. The total intrinsic value of options exercised during the years ended December 31, 2020 was \$0.5 million. There were no options exercised during the year ended December 31, 2019. As of December 31, 2020, the total unrecognized stock-based compensation related to unvested stock option awards granted was \$33.3 million, which the Company expects to recognize over a weighted-average period of approximately 2.7 years.

In January 2021, the Company granted stock options to purchase an aggregate of 1,065,200 shares of common stock pursuant to the 2019 Plan at a weighted-average exercise price of \$19.19 per share and stock options to purchase an aggregate of 126,400 shares of common stock pursuant to the 2020 Inducement Plan at a weighted-average exercise price of \$19.89 per share.

Restricted Stock

In November 2018, in connection with the issuance of the Series A Preferred Stock, the Company's founders agreed to modify their outstanding shares of common stock to include vesting provisions that require continued service to the Company in order to vest in those shares. As such, the 562,500 modified shares of common stock became compensatory upon such modification. The modified shares have a four-year vesting period and a measurement date fair value of \$2.936 per share. For the years ended December 31, 2020 and 2019, 133,593 and 135,350 shares vested, respectively. The total fair value of shares vested during the years ended December 31, 2020 and 2019 was \$0.4 million and \$0.4 million, respectively, which was recorded as stock-based compensation in the consolidated statement of operations. As of December 31, 2020, the total unrecognized compensation expense related to unvested restricted stock was \$0.8 million expected to be recognized over a weighted-average period of approximately 1.9 years.

2019 Employee Stock Purchase Plan

In July 2019, the Company's board of directors and stockholders approved and adopted the 2019 Employee Stock Purchase Plan (the "ESPP"). The ESPP became effective on July 17, 2019. A total of 500,000 shares of common stock were approved to be initially reserved for issuance under the ESPP. In addition, the number of shares of common stock available for issuance under the ESPP will be automatically increased on the first day of each calendar year during the first ten-years of the term of the ESPP, beginning with January 1, 2020 and ending with January 1, 2029, by an amount equal to the lesser of (i) 1% of the outstanding number of shares of common stock on December 31st of the preceding calendar year, (ii) 1,500,000 shares of common stock or (iii) such lesser amount as determined by the Company's board of directors. As of December 31, 2020, 29,876 shares were issued under the ESPP and the Company had 700,023 shares available for future issuance.

Total stock-based compensation is reflected in the consolidated statements of operations as follows (in thousands):

	Year Ended December 31,	
	2020	2019
General and administrative	\$ 7,425	\$ 3,711
Research and development	5,129	2,359
Total	\$ 12,554	\$ 6,070

11. Income Taxes

The Company's losses before income taxes for the years ended December 31, 2020 and 2019 are as follows (in thousands):

	Year Ended December 31,	
	2020	2019
U.S. loss before taxes	\$ (103,371)	\$ (52,654)
Foreign income before taxes	107	122
Loss before income taxes	(103,264)	(52,532)

For the years ended December 31, 2020 and 2019, the Company had a current tax provision of \$6,000 and \$21,000 related to foreign taxes, respectively.

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

	Year Ended December 31,	
	2020	2019
Federal statutory income tax rate	21.00 %	21.00 %
State tax	0.42	(1.62)
Permanent differences	(0.89)	(0.78)
Tax credits	6.42	7.32
Change in valuation allowance	(26.96)	(25.95)
Total tax benefit	<u>(0.01)%</u>	<u>(0.03)%</u>

Significant components of the Company's deferred tax assets are as follows (in thousands):

	December 31,	
	2020	2019
Deferred tax assets:		
Net operating losses	\$ 26,122	\$ 9,486
Tax credit carryforwards	11,294	4,378
Accrued expenses	812	364
Intangibles	5,560	3,570
Lease liability	661	737
Stock-based compensation	2,769	989
Total deferred tax assets	<u>47,218</u>	<u>19,524</u>
Deferred tax liabilities:		
Operating lease right-of-use assets	(385)	(468)
Fixed assets	(184)	(228)
Total deferred tax liabilities	<u>(569)</u>	<u>(696)</u>
Valuation allowance	(46,649)	(18,828)
Net deferred tax assets	<u>\$ —</u>	<u>\$ —</u>

The valuation allowance increased by \$27.8 million and \$13.6 million for the years ended December 31, 2020 and 2019, respectively. The tax benefit of deductible temporary differences or carryforwards is recorded as a deferred tax asset to the extent that management assesses the realization is "more likely than not." Future realization of the tax benefit ultimately depends on the existence of sufficient taxable income within the period available under the tax law. At December 31, 2020 and 2019, the Company has set up valuation allowances against all federal and state net deferred tax assets because based on all available evidence, these deferred tax assets are not more than likely to be realizable.

The Company had federal and state net operating loss carryforwards of approximately \$123.5 million and \$2.6 million at December 31, 2020, and \$44.4 million and \$2.2 million at December 31, 2019, respectively. Federal losses do not expire, and California net operating losses will begin to expire in 2038. The Company also has federal general business credit and California research and development credit carryforwards totaling \$14.5 million and \$0.9 million at December 31, 2020, and \$5.6 million and \$0.3 million at December 31, 2019, respectively. The federal research and development credit carryforwards will begin to expire in 2038, unless previously utilized. The California research credits do not expire.

In general, if the Company experiences a greater than 50 percentage point aggregate change in ownership of certain significant stockholders over a three-year period (a "Section 382 ownership change"), utilization of its pre-change NOL carryforwards and the research and development credit carryforwards is subject to an annual limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, and similar state laws. The annual limitation generally is determined by multiplying the value of the Company's stock at the time of such ownership change, subject to certain adjustments, by the applicable long-term tax-exempt rate. Such limitations may result in expiration of a portion of the NOL carryforwards and research and development credit carryforwards before utilization and may be material. As of December 31, 2020, the Company has not determined to what extent a

potential ownership change will impact the annual limitation that may be placed on the Company's utilization of its NOL carryovers and research and development credit carryforwards.

The Company recognizes the financial statements effects of a tax position when it is more likely than not, based on technical merits, that the position will be sustained upon examination.

A reconciliation of the Company's unrecognized tax benefits is as follows (in thousands):

	<u>Year Ended December 31,</u>	
	<u>2020</u>	<u>2019</u>
Balance at beginning of year	\$ 1,490	\$ 116
(Decrease) related to prior year tax positions	(17)	(20)
Increases related to current year tax positions	2,460	1,394
Balance at end of year	<u>\$ 3,933</u>	<u>\$ 1,490</u>

The Company has considered the amounts and probabilities of the outcomes that can be realized upon ultimate settlement with the tax authorities and determined unrecognized tax benefits primarily related to credits should be established as noted in the summary rollforward above. The unrecognized tax benefits, if recognized and in absence of full valuation allowance, would impact the income tax provision by \$3.6 million and \$1.5 million in 2020 and 2019, respectively. The Company's effective income tax rate would not be impacted if the unrecognized tax benefits are recognized in 2020 and 2019. As of December 31, 2020, the Company does not believe that it is reasonably possible that its unrecognized tax benefits would significantly change in the following 12 months.

The Company is subject to taxation in the United States federal jurisdiction, state jurisdictions and Switzerland. Due to the Company's losses incurred, the Company is subject to the income tax examination by authorities since inception on May 2, 2018. The Company's policy is to recognize interest expense and penalties related to income tax matters as tax expense. As of December 31, 2020, there were no significant accruals for interest related to unrecognized tax benefits or tax penalties.

The Company has not provided U.S. income or foreign withholding taxes on the undistributed earnings of its foreign subsidiaries as of December 31, 2020 and 2019, because it intends to permanently reinvest such earnings outside of the U.S. If these foreign earnings were to be repatriated in the future, the related U.S. tax liability will be immaterial, due to the participation exemption put in place in the Tax Act. We have elected to account for Global Intangible Low-taxed Income (GILTI) as a current period expense when incurred.

12. Contingencies

The Company is subject to potential liabilities under government regulations and various claims and legal actions that are pending or may be asserted from time-to-time. These matters arise in the ordinary course and conduct of the Company's business and may include, for example, commercial, intellectual property, and employment matters. The Company intends to defend itself vigorously in such matters and when warranted, take legal action against others. Furthermore, the Company regularly assesses contingencies to determine the degree of probability and range of possible loss for potential accrual in its financial statements.

An estimated loss contingency is accrued in the Company's financial statements if it is probable that a liability has been incurred and the amount of the loss can be reasonably estimated. The Company does not accrue amounts for liabilities that it does not believe are probable. Litigation is inherently unpredictable, and unfavorable resolutions could occur. As a result, assessing contingencies is highly subjective and requires judgment about future events. During the periods presented, the Company has not recorded any accrual for loss contingencies associated with such government regulations, claims or legal actions, determined that an unfavorable outcome is probable or reasonably possible, or determined that the amount or range of any possible loss is reasonably estimable.

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**

Our management, with the participation and supervision of our Chief Executive Officer and our Chief Financial Officer, have evaluated our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act), as of the end of the period covered by this Annual Report. Based on that evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that as of December 31, 2020, our disclosure controls and procedures were effective to provide reasonable assurance that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in SEC rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure.

Management’s Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Exchange Act Rules 13a-15(f) and 15d-15(f). We maintain internal control over financial reporting designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles.

Internal control over financial reporting cannot provide absolute assurance of achieving financial reporting objectives because of its inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within the Company have been detected. Because of such limitations, there is a risk that material misstatements may not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

Under the supervision and with the participation of our Chief Executive Officer and our Chief Financial Officer, our management conducted an evaluation of the effectiveness of our internal control over financial reporting based on the criteria set forth in “Internal Control—Integrated Framework” issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework). Based on this assessment, our management concluded that our internal control over financial reporting was effective at the reasonable assurance level as of December 31, 2020.

Attestation Report of the Independent Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting due to an exemption established by the JOBS Act for “emerging growth companies” and because we qualify as a “non-accelerated filer” (i.e., we do not qualify as either an “accelerated filer” or a “large accelerated filer” as defined in Rule 12b-2 under the Exchange Act).

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2020 that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item will be contained in our definitive proxy statement to be filed with the Securities and Exchange Commission in connection with our 2021 Annual Meeting of Stockholders (“Definitive Proxy Statement”), which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2020, and is incorporated herein by reference.

Code of Business Conduct and Ethics

We maintain a Code of Conduct that applies to all our employees, officers and directors. This includes our principal executive officer, principal financial officer and principal accounting officer or controller, or persons performing similar functions. The full text of our Code of Conduct is posted on our website at www.mirumpharma.com. If we make any substantive amendments to the Code of Conduct or grant any waiver from a provision of the Code of Conduct to any executive officer or director that are required to be disclosed pursuant to SEC rules, we will promptly disclose the nature of the amendment or waiver on our website or in a current report on Form 8-K.

Item 11. Executive Compensation.

The information required by this item will be set forth in our Definitive Proxy Statement and is incorporated herein by reference.

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

The information required by this item will be set forth in our Definitive Proxy Statement 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 Definitive Proxy Statement and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this item will be set forth in our Definitive Proxy Statement and is incorporated here by reference.

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as part of this Annual Report:

(1) Financial statements

The financial statements filed as part of this Annual Report are included in Part II, Item 8 of this Annual Report.

(2) Financial statement schedules

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

(3) Exhibits

The exhibits listed in the accompanying Exhibit Index are filed as part of, or incorporated by reference into, this Annual Report.

Item 16. Form 10-K Summary

None.

Exhibit Index

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation, as currently in effect (filed as Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed with the SEC on July 25, 2019, and incorporated by reference herein).
3.2	Amended and Restated Bylaws, as currently in effect (filed as Exhibit 3.2 to the Registrant's Current Report on Form 8-K, filed with the SEC on July 25, 2019, and incorporated by reference herein).
4.1	Form of Common Stock Certificate (filed as Exhibit 4.1 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on July 8, 2019, and incorporated by reference herein).
4.2	Investors' Rights Agreement, dated November 5, 2018 (filed as Exhibit 4.2 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on June 21, 2019, and incorporated by reference herein).
4.3	Description of Common Stock of the Registrant (filed as Exhibit 4.3 to the Registrant's Annual Report on Form 10-K, filed with the SEC on March 12, 2020, and incorporated by reference herein).
10.1+	Mirum Pharmaceuticals, Inc. 2018 Equity Incentive Plan (filed as Exhibit 10.1 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on June 21, 2019, and incorporated by reference herein).
10.2+	Forms of grant notice, stock option agreement and notice of exercise under the Mirum Pharmaceuticals, Inc. 2018 Equity Incentive Plan (filed as Exhibit 10.2 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on June 21, 2019, and incorporated by reference herein).
10.3+	Mirum Pharmaceuticals, Inc. 2019 Equity Incentive Plan (filed as Exhibit 10.3 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on July 8, 2019, and incorporated by reference herein).
10.4+	Forms of grant notice, stock option agreement and notice of exercise under the Mirum Pharmaceuticals, Inc. 2019 Equity Incentive Plan (filed as Exhibit 10.4 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on July 8, 2019, and incorporated by reference herein).
10.5+	Forms of restricted stock unit grant notice and award agreement under the Mirum Pharmaceuticals, Inc. 2019 Equity Incentive Plan (filed as Exhibit 10.5 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on July 8, 2019, and incorporated by reference herein).
10.6+	Mirum Pharmaceuticals, Inc. 2019 Employee Stock Purchase Plan (filed as Exhibit 10.6 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on July 8, 2019, and incorporated by reference herein).
10.7+	Mirum Pharmaceuticals, Inc. 2020 Inducement Plan (filed as Exhibit 10.1 to the Registrant's Form 10-Q, filed with the SEC on May 7, 2020, and incorporated by reference herein).
10.8+	Forms of grant notice, stock option agreement and notice of exercise under the Mirum Pharmaceuticals, Inc. 2020 Inducement Plan (filed as Exhibit 10.2 to the Registrant's Form 10-Q, filed with the SEC on May 7, 2020, and incorporated by reference herein).
10.9+	Forms of restricted stock unit grant notice and award agreement under the Mirum Pharmaceuticals, Inc. 2020 Inducement Plan (filed as Exhibit 10.3 to the Registrant's Form 10-Q, filed with the SEC on May 7, 2020, and incorporated by reference herein).
10.10+	Form of Indemnification Agreement by and between the Registrant and each director and executive officer (filed as Exhibit 10.7 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on July 8, 2019, and incorporated by reference herein).
10.11+	Mirum Pharmaceuticals, Inc. Severance Benefit Plan and form of Participation Agreement thereunder (filed as Exhibit 10.8 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on June 21, 2019, and incorporated by reference herein).

Exhibit Number	Description
10.12+	<u>Amended and Restated Offer Letter by and between the Registrant and Michael Grey, dated May 15, 2019, as amended by Letter Agreement by and between the Registrant and Michael Grey, dated December 24, 2019 (filed as Exhibit 10.1 to the Registrant's Current Report on Form 8-K, filed with the SEC on December 27, 2019, and incorporated by reference herein).</u>
10.13+	<u>Amended and Restated Offer Letter by and between the Registrant and Christopher Peetz, dated May 15, 2019 (filed as Exhibit 10.10 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on June 21, 2019, and incorporated by reference herein).</u>
10.14+	<u>Offer Letter by and between the Registrant and Pamela Vig, Ph.D., dated December 1, 2018 (filed as Exhibit 10.11 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on June 21, 2019, and incorporated by reference herein).</u>
10.15+	<u>Offer Letter by and between the Registrant and Lara Longpre, dated December 1, 2018 (filed as Exhibit 10.12 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on June 21, 2019, and incorporated by reference herein).</u>
10.16+	<u>Offer Letter by and between the Registrant and Ian Clements, Ph.D., dated March 4, 2019 (filed as Exhibit 10.13 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on June 21, 2019, and incorporated by reference herein).</u>
10.17+	<u>Offer Letter by and between the Registrant and Edwin J. Tucker, M.D., dated October 21, 2019 (filed as Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, filed with the SEC on November 6, 2019, and incorporated by reference herein).</u>
10.18*	<u>Offer Letter by and between the Registrant and Peter Radovich, dated April 28, 2020.</u>
10.19#	<u>License Agreement by and between Lumena Pharmaceuticals, Inc. and Satiogen Pharmaceuticals, Inc., dated February 8, 2011 (filed as Exhibit 10.15 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on June 21, 2019, and incorporated by reference herein).</u>
10.20#	<u>Amendment to License Agreement by and between Lumena Pharmaceuticals, Inc. and Satiogen Pharmaceuticals, Inc., dated February 8, 2011 (filed as Exhibit 10.16 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on June 21, 2019, and incorporated by reference herein).</u>
10.21#	<u>License Agreement by and between Lumena Pharmaceuticals, Inc. and Pfizer Inc., dated June 1, 2012 (filed as Exhibit 10.17 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on June 21, 2019, and incorporated by reference herein).</u>
10.22#	<u>License Agreement by and between Lumena Pharmaceuticals, Inc. and Sanofi-Aventis Deutschland GmbH, dated September 27, 2012 (filed as Exhibit 10.18 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on June 21, 2019, and incorporated by reference herein).</u>
10.23#	<u>Amendment No. 1 to License Agreement by and between Shire Orphan and Rare Disease GmbH (successor in interest of Lumena Pharmaceuticals, Inc.) and Sanofi-Aventis Deutschland GmbH, dated June 26, 2015 (filed as Exhibit 10.19 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on June 21, 2019, and incorporated by reference herein).</u>
10.24#	<u>Assignment and License Agreement by and between the Registrant and Shire International GmbH, dated November 5, 2018 (filed as Exhibit 10.20 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on June 21, 2019, and incorporated by reference herein).</u>
10.25	<u>Office Lease by and between the Registrant and Hudson Metro Center, LLC, dated January 22, 2019, as amended by First Amendment by and between the Registrant and Hudson Metro Center, LLC, dated June 1, 2019, and as further amended by Second Amendment by and between the Registrant and Hudson Metro Center, LLC, dated November 22, 2019 (filed as Exhibit 10.15 to the Registrant's Registration Statement on Form S-1 (File No. 333-235825) filed with the SEC on January 6, 2020, and incorporated by reference herein).</u>

Exhibit Number	Description
10.26	Sales Agreement by and between the Registrant and SVB Leerink LLC, dated August 3, 2020 (incorporated by reference to Exhibit 1.2 to the Registrant's Registration Statement on Form S-3, as amended (File No. 333-240290), filed with the SEC on August 3, 2020, and incorporated by reference herein).
10.27	Revenue Interest Purchase Agreement by and among the Registrant, the Purchasers from time to time party thereto and Mulholland SA LLC, dated December 8, 2020 (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K, as filed with the SEC on December 10, 2020, and incorporated by reference herein).
10.28	Common Stock Purchase Agreement by and among the Registrant, TPC Investments II LP, TPC Investments Solutions LP and TPC Investments Solutions Co-Invest LP, dated December 8, 2020 (incorporated by reference to Exhibit 99.2 to the Registrant's Current Report on Form 8-K, as filed with the SEC on December 10, 2020, and incorporated by reference herein).
21.1	Subsidiaries of the Registrant (filed as Exhibit 21.1 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-232251), filed with the SEC on June 21, 2019, and incorporated by reference herein).
23.1*	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney. Reference is made to the signature page hereto.
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*†	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2*†	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

* Filed herewith.

+ Indicates management contract or compensatory plan.

Certain portions have been omitted in accordance with 17 CFR § 229.601(b).

† The information in Exhibits 32.1 and 32.2 shall not be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act or the Exchange Act (including this Annual Report), unless the Registrant specifically incorporates the foregoing information into those documents by reference.

SIGNATURES

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

MIRUM PHARMACEUTICALS, INC.

Date: March 9, 2021

By: _____ /s/ Christopher Peetz
Christopher Peetz
President, Chief Executive Officer and Director
(Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Christopher Peetz and Ian Clements, Ph.D. and each of them, as his or her true and lawful attorneys-in-fact and agents, each with the full power of substitution, for him or her and in his or her name, place or stead, 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 all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

Name	Title	Date
<u>/s/ Christopher Peetz</u> Christopher Peetz	President, Chief Executive Officer and Director (Principal Executive Officer)	March 9, 2021
<u>/s/ Ian Clements, Ph.D.</u> Ian Clements, Ph.D.	Chief Financial Officer (Principal Financial and Accounting Officer)	March 9, 2021
<u>/s/ Michael Grey</u> Michael Grey	Director	March 9, 2021
<u>/s/ Tiba Aynechi, Ph.D.</u> Tiba Aynechi, Ph.D.	Director	March 9, 2021
<u>/s/ Laura Brege</u> Laura Brege	Director	March 9, 2021
<u>/s/ Laurent Fischer, M.D.</u> Laurent Fischer, M.D.	Director	March 9, 2021
<u>/s/ Patrick Heron</u> Patrick Heron	Director	March 9, 2021
<u>/s/ Edward T. Mathers</u> Edward T. Mathers	Director	March 9, 2021
<u>/s/ Niall O'Donnell, Ph.D.</u> Niall O'Donnell, Ph.D.	Director	March 9, 2021

MIRUM PHARMACEUTICALS, INC.

April 8, 2020

Peter Radovich
San Mateo, California

Re: Employment Terms

Dear Peter:

It is my pleasure to offer you employment with **MIRUM PHARMACEUTICALS, INC.** (the “**Company**”) on the terms set forth in this offer letter. We are building the premier rare liver disease company and are excited to have you as part of the team.

The terms of the offer are as follows:

Title: Chief Operating Officer

Start Date: April 28, 2020

Responsibilities: You will be responsible for overseeing commercial, corporate development, supply chain and chemistry, manufacturing and control activities at the Company, and you shall perform such duties as are customarily associated with your position. You will report to the President and Chief Executive Officer and will work at the Company’s U.S. headquarters in Foster City.

Annual Salary: Your base salary will be \$410,000 on an annualized basis, less payroll deductions and withholdings, paid on the Company’s normal payroll schedule.

Annual Bonus: You will also be eligible to earn an annual performance bonus, with a target bonus of 40% of your annual base salary, based on the attainment of individual and/or Company objectives, and pro-rated for any partial year of employment. The attainment of such objectives, and the actual amount (if any) of such bonus, will be determined by the Company in its sole discretion, and any such bonus will not be deemed earned unless you are an employee of the Company in good standing on the dates the bonus is determined and paid.

Stock Option Grant: As a material inducement to your acceptance of our offer of employment, subject to approval by the Company’s Board of Directors (the “**Board**”) (or its Compensation Committee), you will be granted a nonqualified stock option to purchase 185,000 shares of the Company’s common stock with an exercise price equal to the fair market value as determined by the Board as of the date of grant (the “**Option**”). The anticipated Option will be governed by the terms and conditions of the Company’s 2020 Inducement Plan (the “**Plan**”) and your grant agreement, and will include a four year vesting schedule, under which 1/4th of the shares vest one year after the vesting commencement date and the balance of the shares vest in a series of 36 successive equal monthly installments measured from the first anniversary of the vesting commencement date, until either the Option is fully vested or your continuous service (as defined in the Plan) terminates, whichever occurs first.

Benefits: You shall be entitled to participate in any of the Company's employee benefit plans or programs that become available to similarly situated employees of the Company to the full extent of your eligibility. A full description of these benefits is available upon request.

Health Insurance: You will be entitled to participate in the Company's health insurance programs to the full extent of your eligibility.

This offer and your continued services are contingent upon a satisfactory proof of your right to work in the United States.

The Company reserves the right to change or otherwise modify, in its sole discretion, any of the preceding terms of employment, including those related to salary, bonus plan, if applicable, and benefits at any time.

As a Company employee, you will be expected to abide by Company rules and policies. These include, but are not limited to, the Company's Code of Conduct, Insider Trading Policy, and Window Period Policy. As a condition of employment, you must sign and comply with the attached Employee Confidential Information and Inventions Assignment Agreement which prohibits unauthorized use or disclosure of the Company's proprietary information, among other obligations.

In your work for the Company, you will be expected not to use or disclose any confidential information, including trade secrets, of any former employer or other person to whom you have an obligation of confidentiality. Rather, you will be expected to use only that information which is generally known and used by persons with training and experience comparable to your own, which is common knowledge in the industry or otherwise legally in the public domain, or which is otherwise provided or developed by the Company. You agree that you will not bring onto Company premises any unpublished documents or property belonging to any former employer or other person to whom you have an obligation of confidentiality. You hereby represent that you have disclosed to the Company any contract you have signed that may restrict your activities on behalf of the Company.

Your employment with the Company will be "at-will." You may terminate your employment with the Company at any time and for any reason whatsoever simply by notifying the Company. Likewise, the Company may terminate your employment at any time, with or without cause or advance notice. Your employment at-will status can only be modified in a written agreement signed by you and by an officer of the Company.

To ensure the rapid and economical resolution of disputes that may arise in connection with your employment with the Company, you and the Company agree that any and all disputes, claims, or causes of action, in law or equity, including but not limited to statutory claims, arising from or relating to the enforcement, breach, performance, or interpretation of this Agreement, your employment with the Company, or the termination of your employment, shall be resolved, to the fullest extent permitted by law, by final, binding and confidential arbitration conducted by JAMS or its successor, under JAMS' then applicable rules and procedures for employment disputes (available upon request and also currently available at <http://www.jamsadr.com/rules-employment-arbitration/>). **You acknowledge that by agreeing to this arbitration procedure, both you and the Company waive the right to resolve any such dispute through a trial by jury or judge or administrative proceeding.** You will have the right to be represented by legal counsel at any arbitration proceeding. The arbitrator shall: (a) have the authority to compel adequate discovery for the resolution of the dispute and to award such relief as would otherwise be permitted by law; and (b) issue a written statement signed by the arbitrator regarding the disposition of each claim and the relief, if any, awarded as to each claim, the reasons for the award, and the arbitrator's essential findings and conclusions on which the award is based. The arbitrator shall be authorized to award all relief that you or the Company would be entitled to seek in a court of law. The Company shall pay all JAMS

arbitration fees in excess of the administrative fees that you would be required to pay if the dispute were decided in a court of law. Nothing in this letter agreement is intended to prevent either you or the Company from obtaining injunctive relief in court to prevent irreparable harm pending the conclusion of any such arbitration.

This letter, together with your Employee Confidential Information and Inventions Assignment Agreement, forms the complete and exclusive statement of your employment agreement with the Company. It supersedes any other agreements or promises made to you by anyone, whether oral or written. Changes in your employment terms, other than those changes expressly reserved to the Company's discretion in this letter, require a written modification signed by an officer of the Company. If any provision of this offer letter agreement is determined to be invalid or unenforceable, in whole or in part, this determination shall not affect any other provision of this offer letter agreement and the provision in question shall be modified so as to be rendered enforceable in a manner consistent with the intent of the parties insofar as possible under applicable law. This letter may be delivered via facsimile, electronic mail (including pdf or any electronic signature complying with the U.S. federal E-SIGN Act of 2000, Uniform Electronic Transactions Act or other applicable law) or other transmission method and shall be deemed to have been duly and validly delivered and be valid and effective for all purposes.

Please sign and date this letter, and the enclosed Employee Confidential Information and Inventions Assignment Agreement and return them to me by April 10, 2020, if you wish to accept employment at the Company under the terms described above. If you accept our offer, we would like you to start on April 28, 2020.

We look forward to your favorable reply and to a productive and enjoyable work relationship.

Sincerely,

/s/ Chris Peetz

Chris Peetz, CEO

Understood and Accepted:

/s/ Peter Radovich

Peter Radovich

4/8/2020

Date

Attachment: Employee Confidential Information and Inventions Assignment Agreement

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. 333-240290) of Mirum Pharmaceuticals, Inc.;
- (2) Registration Statement (Form S-8 No. 333-233502) pertaining to the 2018 Equity Incentive Plan, 2019 Equity Incentive Plan, and 2019 Employee Stock Purchase Plan of Mirum Pharmaceuticals, Inc.; and
- (3) Registration Statement (Form S-8 No. 333-238086) pertaining to the 2019 Equity Incentive Plan, 2019 Employee Stock Purchase Plan, and 2020 Inducement Plan of Mirum Pharmaceuticals, Inc.

of our report dated March 9, 2021, with respect to the consolidated financial statements of Mirum Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2020.

/s/ ERNST & YOUNG LLP

Irvine, California
March 9, 2021

**CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Christopher Peetz, certify that:

1. I have reviewed this Annual Report on Form 10-K of Mirum Pharmaceuticals, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(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 9, 2021

By: _____ /s/ Christopher Peetz
Christopher Peetz
President and Chief Executive Officer
(Principal Executive Officer)

**CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Ian Clements, Ph.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of Mirum Pharmaceuticals, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(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 9, 2021

By: _____
/s/ Ian Clements, Ph.D.
Ian Clements, Ph.D.
Chief Financial Officer
(Principal Financial and Accounting Officer)

**CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report of Mirum Pharmaceuticals, Inc. (the "Company") on Form 10-K for the year ended December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 9, 2021

By: _____ /s/ Christopher Peetz
Christopher Peetz
President and Chief Executive Officer
(Principal Executive Officer)

**CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report of Mirum Pharmaceuticals, Inc. (the "Company") on Form 10-K for the year ended December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 9, 2021

By: _____
/s/ Ian Clements, Ph.D.
Ian Clements, Ph.D.
Chief Financial Officer
(Principal Financial and Accounting Officer)