2018 Annual Report

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2018

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: 001-35668

Intercept Pharmaceuticals, Inc.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**22-3868459**
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)

10 Hudson Yards, 37th Floor
New York, NY 10001
(Address of Principal Executive Offices and Zip Code)
(646) 747-1000
(Registrant's telephone number, including area code)

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

Title of each class	Name of each exchange on which registered
Common Stock, par value $0.001 per share	**Nasdaq Global Select Market**

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

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

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

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

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

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

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

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

The aggregate market value of the registrant's common stock held by non-affiliates as of June 29, 2018, the last business day of the registrant's most recently completed second fiscal quarter, was $1,819.5 million (computed by reference to the closing price of $83.91 on such date as reported by the Nasdaq Global Select Market). Common stock held by our executive officers, directors and certain stockholders as of such date has been excluded from this calculation because such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of shares of the registrant's common stock outstanding as of December 31, 2018 was 29,693,876.

DOCUMENTS INCORPORATED BY REFERENCE

Certain information required by Part III of this Annual Report on Form 10-K is incorporated by reference to the registrant's definitive proxy statement related to its 2019 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

[This page intentionally left blank.]

Intercept Pharmaceuticals, Inc.
Annual Report on Form 10-K
For the Fiscal Year Ended December 31, 2018

TABLE OF CONTENTS

Unless the context otherwise requires, references in this Annual Report on Form 10-K to ''we,'' ''our,'' ''us'' and the ''Company'' refer, collectively, to Intercept Pharmaceuticals, Inc., a Delaware corporation, and its consolidated subsidiaries.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements, including, but not limited to, statements regarding the progress, timing and results of our clinical trials, including our clinical trials for the treatment of nonalcoholic steatohepatitis (''NASH''), the safety and efficacy of our approved product, Ocaliva (obeticholic acid or ''OCA'') for primary biliary cholangitis (''PBC''), and our product development candidates, including OCA for NASH, the timing and acceptance of our potential regulatory filings and potential approval of OCA for NASH or any other indications in addition to PBC, the timing and potential commercial success of OCA and any other product candidates we may develop and our strategy, future operations, future financial position, future revenue, projected costs, financial guidance, prospects, plans, objectives of management and expected market growth.

These statements constitute forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. The words ''anticipate,'' ''believe,'' ''estimate,'' ''expect,'' ''intend,'' ''may,'' ''plan,'' ''predict,'' ''project,'' ''target,'' ''potential,'' ''will,'' ''would,'' ''could,'' ''should,'' ''possible,'' ''continue'' and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of their dates, and we undertake no obligation to update any forward-looking statement except as required by law. These forward-looking statements are based on estimates and assumptions by our management that, although believed to be reasonable, are inherently uncertain and subject to a number of risks.

The following represent some, but not necessarily all, of the factors that could cause actual results to differ materially from historical results or those anticipated or predicted by our forward-looking statements:

- our ability to successfully commercialize Ocaliva for PBC;
- our ability to maintain our regulatory approval of Ocaliva for PBC in the United States, Europe, Canada, Israel, Australia and other jurisdictions in which we have or may receive marketing authorization;
- the initiation, timing, cost, conduct, progress and results of our research and development activities, preclinical studies and clinical trials, including any issues, delays or failures in identifying patients, enrolling patients, treating patients, meeting specific endpoints in the jurisdictions in which we intend to seek approval or completing and timely reporting the results of our NASH or PBC clinical trials;
- our ability to timely and cost-effectively file for and obtain regulatory approval of our product candidates, including OCA for NASH, in the United States, Europe and our other target markets;
- conditions that may be imposed by regulatory authorities on our marketing approvals for our products and product candidates, such as the need for clinical outcomes data (and not just results based on achievement of a surrogate endpoint), and any related restrictions, limitations and/or warnings contained in the label of any of our products or product candidates;
- any potential side effects associated with Ocaliva for PBC, OCA for NASH or our other product candidates that could delay or prevent approval, require that an approved product be taken off the market, require the inclusion of safety warnings or precautions or otherwise limit the sale of such product or product candidate;
- our ability to establish and maintain relationships with, and the performance of, third-party manufacturers, contract research organizations and other vendors upon whom we are substantially dependent for, among other things, the manufacture and supply of our products, including Ocaliva for PBC and, if approved, OCA for NASH, and our clinical trial activities;
- our ability to identify, develop and successfully commercialize our products and product candidates, including our ability to timely and successfully launch OCA for NASH, if approved;

- our ability to obtain and maintain intellectual property protection for our products and product candidates, including our ability to cost-effectively file, prosecute, defend and enforce any patent claims or other intellectual property rights;
- the size and growth of the markets for our products and product candidates and our ability to serve those markets;
- the degree of market acceptance of Ocaliva for PBC and, if approved, OCA for NASH or our other product candidates among physicians, patients and healthcare payors;
- the availability of adequate coverage and reimbursement from governmental and private healthcare payors for our products, including Ocaliva for PBC and, if approved, OCA for NASH, and our ability to obtain adequate pricing for such products;
- our ability to establish and maintain effective sales, marketing and distribution capabilities, either directly or through collaborations with third parties;
- competition from existing drugs or new drugs that become available;
- our ability to prevent system failures, data breaches or violations of data protection laws;
- costs and outcomes relating to any disputes, governmental inquiries or investigations, legal proceedings or litigation, including any securities, intellectual property, employment, product liability or other litigation;
- our collaborators' election to pursue research, development and commercialization activities;
- our ability to establish and maintain relationships with collaborators with development, regulatory and commercialization expertise;
- our need for and ability to generate or obtain additional financing;
- our estimates regarding future expenses, revenues and capital requirements and the accuracy thereof;
- our use of cash and short-term investments;
- our ability to acquire, license and invest in businesses, technologies, product candidates and products;
- our ability to attract and retain key personnel to manage our business effectively;
- our ability to manage the growth of our operations, infrastructure, personnel, systems and controls;
- our ability to obtain and maintain adequate insurance coverage;
- the impact of general U.S. and foreign economic, industry, market, regulatory or political conditions, including the potential impact of Brexit; and
- the other risks and uncertainties identified under the captions ''Risk Factors,'' ''Business'' and ''Management's Discussion and Analysis of Financial Condition and Results of Operations'' and elsewhere in this Annual Report on Form 10-K and in our other periodic filings filed with the U.S. Securities and Exchange Commission.

NOTE REGARDING TRADEMARKS

The Intercept Pharmaceuticals® name and logo and the Ocaliva® name and logo are either registered or unregistered trademarks or trade names of the Company in the United States and/or other countries. All other trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners. Solely for convenience, trademarks and trade names referred to in this Annual Report on Form 10-K may appear without the® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights to these trademarks and trade names.

[This page intentionally left blank.]

PART I

Item 1. Business

Overview

We are a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat progressive non-viral liver diseases with high unmet medical need utilizing our proprietary bile acid chemistry. Our first marketed product, Ocaliva® (obeticholic acid or ''OCA''), is an farnesoid X receptor (''FXR'') agonist approved in the United States, the European Union and several other jurisdictions for the treatment of primary biliary cholangitis (''PBC'') in combination with ursodeoxycholic acid (''UDCA'') in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA. In addition to commercializing OCA for PBC under the Ocaliva brand name, we are currently developing OCA for multiple indications, including nonalcoholic steatohepatitis (''NASH''). We are also developing several other product candidates in various stages of clinical and preclinical development. We believe that OCA and our other product candidates have the potential to treat orphan and other more prevalent liver diseases such as NASH for which there are currently limited therapeutic options.

Ocaliva was approved for PBC by the U.S. Food and Drug Administration (''FDA'') in May 2016 under the accelerated approval pathway. We commenced sales and marketing of Ocaliva in the United States shortly after receiving approval, and Ocaliva is now available to U.S. patients primarily through a network of specialty pharmacy distributors. Ocaliva received conditional approval for PBC from the European Commission in December 2016 and we commenced our European commercial launch in January 2017. We have submitted dossiers and obtained, or are otherwise pursuing, reimbursement from a number of national authorities in Europe. Since January 2017, Ocaliva has also received regulatory approval in several of our target markets outside the United States and Europe, including Canada, Israel and Australia, and we are pursuing marketing approval of Ocaliva for PBC in our other international target markets. Ocaliva received orphan drug designation in both the United States and the European Union for the treatment of PBC.

Our lead product candidate is OCA for the potential treatment of NASH. In February 2019, we announced topline results from the planned 18-month interim analysis of our pivotal Phase 3 clinical trial of OCA in patients with liver fibrosis due to NASH, known as the REGENERATE trial. In the primary efficacy analysis, once-daily OCA 25 mg met the primary endpoint agreed with the FDA of fibrosis improvement by at least one stage with no worsening of NASH at the planned 18-month interim analysis and adverse events were generally mild to moderate in severity and the most common were consistent with the known profile of OCA. OCA also achieved the primary endpoint in a Phase 2b clinical trial for the treatment of NASH completed in late July 2014, known as the FLINT trial, which was sponsored by the U.S. National Institute of Diabetes and Digestive and Kidney Diseases (''NIDDK''), a part of the National Institutes of Health. OCA has received breakthrough therapy designation from the FDA for the treatment of NASH patients with liver fibrosis. We currently intend to file for approval of OCA for NASH in the United States and Europe in the second half of 2019. We also continue to work towards expanding our overall NASH development program with additional trials and studies, including our ongoing Phase 3 trial in NASH patients with compensated cirrhosis, known as the REVERSE trial.

As part of our product development activities, we expect to continue to invest in evaluating the potential of OCA in other progressive non-viral liver diseases beyond PBC and NASH. We also intend to study OCA in combination with bezafibrate, a pan-peroxisome proliferator-activated receptor (''PPAR'') agonist, in patients with PBC and potentially other liver diseases. In addition, we have a pipeline of additional compounds in early stages of research and development.

Liver Function, Bile Acids and Progressive Non-Viral Liver Diseases

The liver performs many functions that are vital for maintaining health, including the regulation of bile acid metabolism. Bile acids are natural detergent-like emulsifying agents that are released from the gallbladder into the intestine when food is ingested, and are essential for the absorption of dietary cholesterol and other nutrients. Cholesterol bound by bile acids is taken up by the liver, where the cholesterol is then converted into one of two primary bile acids. The bile acids are then actively secreted into bile ducts, which eventually empty into the gallbladder. This digestive cycle of bile flow from gallbladder to intestine to liver and back is called the enterohepatic recirculation of bile.

In addition to facilitating nutrient absorption, bile acids act as important signals that help regulate multiple other biological functions. They are also complex signaling molecules that integrate metabolic and immune pathways involved in the healthy functioning of various tissues and organs. For example, the actions of bile acids in the liver, intestine and kidney regulate repair mechanisms that modulate inflammation and fibrosis (scarring), which can lead to progressive organ damage.

The biological effects of bile acids are mediated through dedicated receptors. The best understood receptor is FXR, a nuclear receptor that regulates bile acid synthesis and clearance from the liver, thereby preventing excessive bile acid build-up in the liver, which may be toxic. As such, FXR is a target for the treatment of several liver diseases such as PBC that involve impaired bile flow, a condition called cholestasis. In cholestasis, the liver is typically exposed to higher than normal levels of bile acids, which can cause significant damage over time. In addition, bile acid activation of FXR induces anti-fibrotic, anti-inflammatory, anti-steatotic and other mechanisms that are necessary for the normal regeneration of the liver. As a result, FXR is also a target for the treatment of more common liver diseases such as NASH and alcoholic hepatitis. Further, based on the discovery of similar FXR-mediated protective mechanisms in other organs exposed to bile acids, we believe that FXR may also be a potential target for the treatment of a number of intestinal, kidney and other diseases.

OCA is a bile acid analog, a chemical substance that has a structure based on a naturally occurring human bile acid, that selectively binds to and activates FXR. We believe that OCA has broad liver-protective properties and may effectively counter a variety of chronic insults to the liver that cause fibrosis (scarring), which can eventually lead to cirrhosis, liver transplant and death. Due to OCA's bile acid-like properties, it circulates enterohepatically and engages FXR in both the liver and intestine. FXR engagement in the liver is believed to be critical to successfully treat pathologic injury due to progressive underlying disease.

By virtue of our patent portfolio and the proprietary know-how of our employees and collaboration partners, we believe that we hold a leading position in the fields of bile acid chemistry and therapeutics. Our research and development efforts have resulted in a pipeline of bile acid analogs in addition to OCA and through our on-going work with our collaboration partners such as Professor Roberto Pellicciari, Ph.D., one of our co-founders, and TES Pharma S.r.l., we are continuing our research to rationally design compounds that bind selectively and potently to FXR and other bile acid receptors.

Our Strategy

Our objective is to develop and commercialize novel therapeutics for the treatment of progressive non-viral liver diseases with high unmet medical need. The key elements of our strategy are to:

- *Advance our leading NASH program.* Based on the positive topline results from the 18-month analysis of our pivotal Phase 3 REGENERATE trial in patients with liver fibrosis due to NASH, we currently intend to file for approval of OCA for NASH in the United States and Europe in the second half of 2019 and will continue to prepare for the potential commercialization of OCA for NASH, if approved. We also expect to continue REGENERATE through clinical outcomes and to progress our Phase 3 REVERSE trial for NASH patients with compensated cirrhosis. We may also conduct studies to explore the potential of OCA in combination therapy.
- *Grow our global PBC business.* We intend to grow our global net sales of Ocaliva to eligible patients by increasing Ocaliva's market access and penetration in the markets where Ocaliva has been approved, pursuing regulatory approval for Ocaliva in our target markets where Ocaliva has not yet been approved and developing additional innovative product candidates, such as OCA in combination with bezafibrate, for PBC.
- *Develop and expand our pipeline.* We intend to continue to develop OCA and our other existing product candidates, alone or in combination, for non-viral liver diseases in indications beyond NASH and PBC. In addition, we intend to expand our portfolio of clinical and preclinical product candidates by leveraging our and our collaborators' expertise in bile acid chemistry and opportunistically pursuing business development transactions.

- *Expand and protect our intellectual property.* We intend to expand and aggressively prosecute our intellectual property in the area of bile acid chemistry and therapeutics with the objective of maintaining a defensible and valuable intellectual property portfolio.

History and Development of the Company

In September 2002, we were incorporated in Delaware and shortly thereafter began operations in New York. In October 2012, following several rounds of private funding, we completed our initial public offering (the ''IPO'') and received net proceeds of approximately $78.7 million therefrom. We used the proceeds from our IPO to fund, among other things, preclinical and clinical development activities, including our Phase 3 POISE trial studying OCA for PBC and work performed in anticipation of our submission of regulatory filings for the approval of OCA for PBC. In addition, between June 2013 and April 2015, we completed four registered public offerings of our common stock and received aggregate net proceeds of approximately $803.4 million therefrom.

In March 2014, we announced the results of our Phase 3 POISE trial of OCA for PBC. In November 2014, results from the FLINT Phase 2b clinical trial of OCA for NASH were published in *The Lancet*. Both of these trials met their primary endpoints.

In June 2015, we completed submission of a New Drug Application (''NDA'') to the FDA for accelerated approval of OCA for PBC and a Marketing Authorization Application (''MAA'') to the European Medicines Agency (''EMA'') for conditional approval of OCA for PBC. In September 2015, we announced the initiation of our Phase 3 REGENERATE trial of OCA in patients with liver fibrosis due to NASH.

In May 2016, Ocaliva was approved for PBC by the FDA. We commenced sales and marketing of Ocaliva in the United States shortly after receiving approval. In July 2016, we issued and sold $460.0 million aggregate principal amount of 3.25% Convertible Senior Notes due 2023 (the ''Convertible Notes'') in a registered public offering and received net proceeds of approximately $447.6 million therefrom. In December 2016, Ocaliva received conditional approval for PBC from the European Commission.

In January 2017, we commenced our European launch of Ocaliva for PBC. Since January 2017, Ocaliva has also received regulatory approval in several of our target markets outside the United States and Europe, including Canada, Israel and Australia, and we are pursuing marketing approval of Ocaliva for PBC in our other international target markets. In July 2017, we announced positive results from our Phase 2 CONTROL trial, the goal of which was to characterize the lipid metabolic effects of OCA and cholesterol management effects of concomitant statin administration in NASH patients, as well as positive topline results from our Phase 2 AESOP trial of OCA for primary sclerosing cholangitis (''PSC'').

In February 2018, we announced our Phase 3 REVERSE trial of OCA for NASH patients with compensated cirrhosis. In April 2018, we issued and sold an aggregate of approximately 4.3 million shares of common stock in a registered public offering and a concurrent private placement (the ''Concurrent Private Placement'') exempt from the registration requirements of the Securities Act of 1933, as amended, and received net proceeds of approximately $261.4 million therefrom. In December 2018, we entered into an agreement (the ''Aralez Agreement'') with Aralez Pharmaceuticals Canada Inc. (''Aralez''), pursuant to which we acquired (i) Aralez's license to develop and commercialize bezafibrate in the United States, (ii) Aralez's investigational new drug application (''IND'') on file with the FDA and other associated regulatory documentation and (iii) a non-exclusive license to certain of Aralez's intellectual property. We intend to evaluate the efficacy, safety and tolerability of bezafibrate in combination with OCA in patients with PBC in a Phase 2 study, with the longer-term goal of developing and seeking regulatory approval for a fixed dose combination regimen in this indication and potentially other liver diseases.

In February 2019, we announced topline results from our pivotal Phase 3 REGENERATE trial in patients with liver fibrosis due to NASH. In the primary efficacy analysis, once-daily OCA 25 mg met the primary endpoint agreed with the FDA of fibrosis improvement by at least one stage with no worsening of NASH at the planned 18-month analysis and adverse events were generally mild to moderate in severity and the most common were consistent with the known profile of OCA.

For information regarding our financial condition and results of operations, including our revenues, net loss and total assets, see our audited consolidated financial statements and accompanying notes and

‘‘Management’s Discussion and Analysis of Financial Condition and Results of Operations’’ included elsewhere in this Annual Report on Form 10-K.

Our First Approved Product

Ocaliva

Ocaliva was approved for PBC by the FDA in May 2016 under the accelerated approval pathway. We commenced sales and marketing of Ocaliva in the United States shortly after receiving approval, and Ocaliva is now available to U.S. patients primarily through a network of specialty pharmacy distributors. Ocaliva received conditional approval for PBC from the European Commission in December 2016 and we commenced our European commercial launch in January 2017. We have submitted dossiers and obtained, or are otherwise pursuing, reimbursement from a number of national authorities in Europe. Since January 2017, Ocaliva has also received regulatory approval in several of our target markets outside the United States and Europe, including Canada, Israel and Australia, and we are pursuing marketing approval of Ocaliva for PBC in our other international target markets. Ocaliva received orphan drug designation in both the United States and the European Union for the treatment of PBC.

Overview of PBC

PBC is a rare liver disease that primarily results from autoimmune destruction of the bile ducts that transport bile acids out of the liver, resulting in cholestasis. The build-up of bile acids in the liver damages liver cells. These damaged liver cells, in turn, release abnormal amounts of serum alkaline phosphatase (‘‘ALP’’), a liver enzyme that is a key biomarker of the disease pathology. As shown in numerous clinical trials of treatment with UDCA (available generically as ursodiol), a positive therapeutic response is primarily determined by sustained reduction of ALP levels, along with maintenance of normal bilirubin levels, indicating adequately compensated liver function. This biochemical improvement has been shown to correlate well with improved clinical outcomes such as transplant-free survival. As the disease progresses, it causes progressive liver damage marked by chronic inflammation and fibrosis. Despite its rarity, PBC is the most common cholestatic liver disease and is the second leading indication for liver transplant among women in the United States. Disease progression in PBC varies significantly, with median survival in untreated patients of 7.5 years if symptomatic at diagnosis and up to 16 years if asymptomatic at diagnosis. PBC patients whose disease is progressing have persistently elevated levels of ALP and other liver enzymes, with abnormal bilirubin levels heralding more advanced disease. Data from published long-term studies demonstrate that a significant portion of such patients with advancing disease progress to liver failure, transplant or death within five to ten years.

According to our analysis of 2016 industry data, there are approximately 290,000 people with PBC in the United States, certain European countries, Canada, Australia and New Zealand. An estimated 90% of PBC patients are women, with approximately one in 1,000 women over the age of 40 afflicted by the disease. The mean age of diagnosis is about 40 years and the typical initial presentation occurs between the ages of 30 and 65 years. A majority of PBC patients are asymptomatic at the time of initial diagnosis, but most develop symptoms over time. Fatigue and pruritus are the most common symptoms in PBC patients. Less common symptoms include dry eyes and mouth, as well as jaundice, which can be seen in more advanced disease. Based on the guidelines of the American Association for the Study of Liver Disease and the European Association for the Study of the Liver, the clinical diagnosis of PBC is established based on the presence of (i) a positive antimitochondrial antibody (‘‘AMA’’), a marker of this autoimmune disease seen in up to 95% of PBC patients and (ii) elevated serum levels of ALP. In the earlier stages of PBC, ALP is often the only abnormally elevated liver enzyme, rising to between two to ten times higher than normal values. Bilirubin is a marker of liver function and is also monitored in PBC to provide an indication of how well the liver is functioning. Liver biopsy can be used to confirm the diagnosis of PBC, but is not required and is becoming less-frequently performed.

A number of published clinical studies have demonstrated that lower levels of ALP, both independently or in conjunction with normal bilirubin levels, correlate with a significant reduction in adverse clinical outcomes such as liver transplant and/or death in PBC patients. These studies include the result of meta-analyses of PBC clinical outcomes data of more than 6,000 PBC patients from 15 academic centers in

eight countries that have been compiled by the Global PBC Study Group, which we sponsored, as well as a dataset of over 6,000 PBC patients across the United Kingdom compiled by the UK PBC Group.

Prior to Ocaliva, the only approved drug indicated for the treatment of PBC was UDCA, which is widely considered the standard first-line therapy for PBC patients. In patients for whom UDCA is effective, the treatment slows the progression of PBC, reducing the likelihood of liver failure and the need for transplant.

Phase 3 POISE Trial

Ocaliva's accelerated approval in the United States and conditional approval in the European Union was supported by the results of our Phase 3 POISE trial, which was completed in March 2014. The data from the POISE trial showed that Ocaliva, at both a once-daily 10 mg dose and a once-daily 5 mg dose titrated to 10 mg, met the trial's primary endpoint of achieving a reduction in ALP to below a threshold of 1.67 times the upper limit of normal (''ULN''), with a minimum of a 15% reduction in ALP level from baseline, and a normal bilirubin level after 12 months of therapy. The percentage of patients meeting the POISE trial's primary endpoint was 10% in the placebo group, 47% in the 10 mg Ocaliva group and 46% in the Ocaliva titration group (both dose groups $p < 0.0001$ as compared to placebo) in an intent-to-treat analysis. The placebo group experienced a mean decrease in ALP from baseline of 5%, compared to a mean decrease of 39% in the 10 mg Ocaliva dose group and 33% in the Ocaliva titration group (both dose groups $p < 0.0001$ as compared to placebo). Pruritus, generally mild to moderate, was the most frequently reported adverse event associated with Ocaliva treatment and was observed in 38% of patients on placebo, 70% of patients in the 10 mg Ocaliva group and 56% of patients in the Ocaliva titration group. Eight patients discontinued due to pruritus, of whom none were in the placebo group, seven (10%) were in the 10 mg Ocaliva group and one (1%) was in the Ocaliva titration group. Decreases in high density lipoprotein (''HDL'') cholesterol were also observed during treatment. Following the completion of the double-blind portion of the POISE trial described above, patients were given the option to enroll in an open-label long-term safety and efficacy extension trial.

Ongoing Confirmatory Clinical Outcomes Trial and Other Post Marketing Requirements

In connection with Ocaliva's accelerated approval in the United States and conditional approval in the European Union, we committed to conduct a Phase 4 confirmatory outcomes trial of Ocaliva, known as the COBALT trial, and other clinical trials to satisfy post-marketing regulatory requirements. We have agreed to evaluate the safety and efficacy of Ocaliva in patients with moderate to severe hepatic impairment and as a monotherapy in patients with PBC. In addition, we have agreed to develop and characterize a lower dose formulation of Ocaliva to allow for once daily dosing in patients with moderate or advanced hepatic impairment. Continued approval of Ocaliva for PBC in the United States, the European Union and other jurisdictions may be contingent upon the verification and description of clinical benefit in confirmatory trials.

The goal of the COBALT trial is to confirm that reduction of ALP with OCA treatment is associated with a longer-term benefit on liver-related clinical outcomes. This trial is currently enrolling patients and is expected to be completed on a post-marketing basis. COBALT is designed to assess the effect of a once-daily dose of 5 mg or 10 mg of Ocaliva in approximately 430 PBC patients with an inadequate therapeutic response to UDCA or who are unable to tolerate UDCA. In this trial, eligible patients with PBC continue their UDCA treatment, except for those patients unable to tolerate UDCA, and are being randomized into one of two treatment arms of approximately 215 patients each. Patients are randomized to receive either (i) placebo or (ii) Ocaliva starting at 5 mg and increasing over the course of the trial to 10 mg of Ocaliva based on tolerability. Dosing frequency will be determined by disease stage. The primary endpoint of the trial is based on clinical outcomes as measured by time to first occurrence of any of the following adjudicated events: death (all-cause), liver transplant, Model of End Stage Liver Disease (''MELD'') score greater than 15, hospitalization due to variceal bleeding, encephalopathy or spontaneous bacterial peritonitis, uncontrolled ascites or hepatocellular carcinoma. The study evaluates subjects across the spectrum of PBC disease, including early and advanced PBC.

Ocaliva Label Update

In the course of our post-marketing pharmacovigilance activities, deaths have been reported in PBC patients with moderate or severe hepatic impairment. In an analysis performed by us and in consultation with the FDA, we concluded that certain of these patients were prescribed once daily doses of Ocaliva, which is seven times higher than the recommended weekly dose in such patients. As a result, in September 2017, we

issued a Dear Health Care Provider (“DHCP”) letter, and the FDA also subsequently issued its own drug safety communication to reinforce recommended label dosing. Both communications remind healthcare providers of the importance of the recommended reduced dosing of Ocaliva in PBC patients with moderate or severe hepatic impairment, while reiterating the importance of monitoring PBC patients for progression of their disease and the occurrence of liver-related adverse reactions. In addition to the DHCP letter, we took actions to enhance education about appropriate use of Ocaliva. These initiatives included: reeducating physicians on the label, with a focus on ensuring appropriate dosing for patients with moderate or severe hepatic impairment; enhancing monitoring of patients for liver-related adverse reactions; and adjudicating reported cases of serious liver injury, including in patients with no or mild hepatic impairment.

In February 2018, we announced that the Ocaliva label in the United States had been updated by the FDA to include a boxed warning and a dosing table that reinforced the then-existing dosing schedule for patients with Child-Pugh Class B or C or decompensated cirrhosis. In addition, the FDA issued an updated drug safety communication to accompany the revised label. We remain focused on the safety of all of the patients using Ocaliva within and outside of our ongoing clinical studies and have engaged with relevant regulatory authorities to ensure that the Ocaliva label sufficiently reinforces the importance of appropriate dosing in patients with advanced cirrhosis.

Our Product Candidates

The following summarizes the current status and the anticipated next steps in our development plans for our product candidates. We continually evaluate each product candidate in an effort to efficiently allocate research and development dollars to projects we deem to be in our best interests based on, among other factors, the product candidate’s performance in pre-clinical and/or clinical studies, our expectations regarding the potential future regulatory approval of the product candidate and our view of the potential commercial viability of the product candidate in light of market conditions.

OCA for NASH

Our lead product candidate is OCA for the potential treatment of NASH. In February 2019, we announced topline results from our pivotal Phase 3 clinical trial of OCA in patients with liver fibrosis due to NASH, known as the REGENERATE trial. In the primary efficacy analysis, once-daily OCA 25 mg met the primary endpoint agreed with the FDA of fibrosis improvement by at least one stage with no worsening of NASH at the planned 18-month interim analysis and adverse events were generally mild to moderate in severity and the most common were consistent with the known profile of OCA. OCA has received breakthrough therapy designation from the FDA for the treatment of NASH patients with liver fibrosis. We currently intend to file for approval of OCA for NASH in the United States and Europe in the second half of 2019. We also are conducting a Phase 3 trial in NASH patients with compensated cirrhosis, known as the REVERSE trial.

Overview of NASH

NASH is a serious progressive liver disease caused by excessive fat accumulation in the liver (steatosis) that induces chronic inflammation, resulting in progressive fibrosis (scarring) that can lead to cirrhosis, eventual liver failure, cancer and death. More than 20% of patients with NASH progress to cirrhosis within a decade of diagnosis and, compared to the general population, have a ten-fold greater risk of liver-related mortality. The proportion of liver transplants attributable to NASH has increased rapidly in recent years and as early as 2020 the disease is projected to become the leading cause of liver transplants in the United States. Additionally, NASH is now considered to be a leading, and a rapidly increasing, cause of hepatocellular carcinoma (primary liver cancer), of which up to 40% of cases in NASH patients develop prior to developing cirrhosis.

Although difficult to precisely estimate, current epidemiology research estimates that the global prevalence of NASH is approximately 3 – 5% and is expected to increase markedly by 2030. Fibrosis is the most robust predictor of long-term overall mortality, liver transplantation and liver-related events in patients with NASH and advanced fibrosis is associated with a substantially higher risk of liver-related morbidity and mortality in patients with NASH. We believe that a majority of NASH patients diagnosed and under treater care have fibrosis of stage 2 or greater. Although the prevalence of NASH is lower in children, it has also

become a serious disease burden in the pediatric population. Other common co-existing conditions such as obesity and type 2 diabetes, which are present in a majority of NASH patients, raise important risks. NASH has been linked in both developed and developing countries to the adoption of a Western diet, with increased consumption of processed foods containing polyunsaturated fatty acids and fructose.

Currently, a definitive diagnosis of NASH requires a histologic assessment of a liver biopsy for several key features associated with NASH, including, but not limited to, steatosis, lobular inflammation and hepatocyte ballooning. However, we believe that the majority of NASH patients under treater care have been diagnosed and found specialist care without a liver biopsy. Several imaging and circulating biomarkers are being investigated as non-invasive diagnostic methods, including transient elastography (an ultrasound technology approved in the United States and Europe for the measurement of liver fibrosis), magnetic resonance imaging and serum biomarkers. NASH diagnosis rates in the United States and the EU5 countries are very low, owing to a lack of approved treatment options and a lack of validated non-invasive diagnosis options. We believe the availability of novel therapeutics and non-invasive technologies will be instrumental in improving diagnosis rates.

There are currently no medications approved for the treatment of NASH. However, various therapeutics are used off-label, such as vitamin E (an antioxidant), insulin sensitizers (e.g., metformin, pioglitazone), antihyperlipidemic agents (e.g., gemfibrozil), pentoxifylline and UDCA. Lifestyle changes, including modification of diet and exercise to reduce body weight, as well as treatment of concomitant diabetes and dyslipidemia, are commonly accepted as the standard of care, but have not conclusively been shown to prevent disease progression. Although some of the off-label treatments described above have been studied as possible treatments for NASH, none has been approved by the FDA or EMA as a treatment for this disease. Currently, treatment options for NASH patients with advanced cirrhosis are limited. Although liver transplant can be life-saving, many patients fail to receive a donor organ in time, and for those who do, there are very significant clinical risks, such as infection and organ rejection, as well as significant costs. In addition, the post-transplant recurrence rate of NASH has been shown to be as high as 25% at 18 months. Given the lack of available treatment options, we believe that there is a significant unmet need for novel therapies for NASH, particularly in those patients with advanced fibrosis and cirrhosis and those with a high risk of disease progression due to other co-morbidities such as type 2 diabetes.

FXR activation has been shown to play a key role in the regulation of the metabolic pathways relevant to NASH, highlighting FXR as a potential drug target for treatment of the disease. Given the significant unmet medical need of patients with NASH, we believe that the ability of OCA to potently activate FXR has the potential to convey clinical benefit by improving key histologic parameters of the disease. This is supported by preclinical and clinical results obtained to date, and further investigated in our ongoing clinical trial program.

Phase 3 REGENERATE Trial

We are currently conducting a pivotal Phase 3 clinical trial of OCA in patients with liver fibrosis due to NASH, known as the REGENERATE trial. REGENERATE is a randomized, double-blind, placebo-controlled, multicenter study assessing the safety and efficacy of OCA on liver-related clinical outcomes in patients with liver fibrosis due to NASH. Patients with biopsy proven NASH with fibrosis are randomized 1:1:1 to receive placebo, OCA 10 mg or OCA 25 mg once daily.

An 18-month analysis was conducted to assess the effect of OCA in liver histology comparing month 18 biopsy with baseline. Patients without a repeat biopsy due to study discontinuation or other reason were treated as non-responders in the primary efficacy analysis and full efficacy analysis (each as described below). REGENERATE is targeted to enroll more than 2,000 adult NASH patients with stage 2 and 3 fibrosis across 339 qualified centers worldwide. A smaller exploratory cohort of 287 patients with stage 1 liver fibrosis and at least one accompanying comorbidity (specified as diabetes, obesity or alanine transaminase (‘‘ALT’’) greater than 1.5 times ULN) were also enrolled in REGENERATE, but were not included in the primary efficacy analysis. As described below, these patients were included in the full efficacy analysis and safety analysis. REGENERATE is planned to continue through clinical outcomes in order to confirm clinical benefit. The end-of-study analysis will evaluate the effect of OCA on mortality and liver-related clinical outcomes, as well as its long-term safety.

In February 2019, we announced topline results from the REGENERATE trial. In the primary efficacy analysis, once-daily OCA 25 mg met, with statistical significance, the primary endpoint agreed with the FDA of fibrosis improvement by at least one stage with no worsening of NASH (defined as no worsening of hepatocellular ballooning, no worsening of lobular inflammation and no worsening of steatosis) at the planned 18-month analysis and adverse events were generally mild to moderate in severity and the most common were consistent with the known profile of OCA. Although a numerically greater proportion of patients in both OCA treatment arms compared to placebo achieved the primary endpoint of NASH resolution with no worsening of liver fibrosis in the primary efficacy analysis, this result did not reach statistical significance. NASH resolution is defined as the overall histopathologic interpretation of (i) no fatty liver disease or (ii) fatty liver disease (simple or isolated steatosis) without steatohepatitis AND a nonalcoholic fatty liver disease (''NAFLD'') activity score (''NAS'') of 0 for ballooning and 0-1 for inflammation. As agreed with the FDA, in order for the primary objective to be met, the study was required to achieve one of the two primary endpoints.

The ''primary efficacy analysis'' (Intent-to-Treat or ''ITT'') assessed efficacy at 18 months in 931 patients with stage 2 or 3 liver fibrosis due to NASH. Overall study discontinuations in the primary efficacy analysis population were balanced across treatment arms: 16% in placebo, 17% in OCA 10 mg and 15% in OCA 25 mg. An additional pre-specified ''full efficacy analysis'' at 18 months added an exploratory cohort of 287 NASH patients with stage 1 liver fibrosis and additional risk factors who were at increased risk of progression to cirrhosis (N = 1,218).

Set forth below is a summary of the 18-month primary efficacy analysis and additional full efficacy analysis from the REGENERATE trial.

Fibrosis Improvement at Month 18

Primary Efficacy Analysis (ITT population: NASH with stage 2 and 3 liver fibrosis)	**Placebo n = 311**	**OCA 10 mg n = 312**	**OCA 25 mg n = 308**
Fibrosis improvement (≥ 1 stage) with no worsening of NASH*	**11.9%**	**17.6% p = 0.0446**	**23.1% p = 0.0002****
Additional Full Efficacy Analysis (ITT population plus stage 1 liver fibrosis patients)	Placebo n = 407	OCA 10 mg n = 407	OCA 25 mg n = 404
Fibrosis improvement (≥ 1 stage) with no worsening of NASH*	10.6%	15.7% p = 0.0286	21.0% p < 0.0001
* Defined as no worsening of hepatocellular ballooning, no worsening of lobular inflammation and no worsening of steatosis. ** Statistically significant in accordance with the statistical analysis plan agreed with the FDA.			

NASH Resolution at Month 18

Primary Efficacy Analysis (ITT population: NASH with stage 2 and 3 liver fibrosis)	**Placebo n = 311**	**OCA 10 mg n = 312**	**OCA 25 mg n = 308**
NASH resolution‡ with no worsening of liver fibrosis stage	**8.0%**	**11.2% p = 0.1814**	**11.7% p = 0.1268**
Additional Full Efficacy Analysis (ITT population plus stage 1 liver fibrosis patients)	Placebo n = 407	OCA 10 mg n = 407	OCA 25 mg n = 404
NASH resolution‡ with no worsening of liver fibrosis stage	7.9%	11.3% p = 0.0903	14.9% p = 0.0013
‡ Defined as the overall histopathologic interpretation of (i) no fatty liver disease or (ii) fatty liver disease (simple or isolated steatosis) without steatohepatitis AND a NAS of 0 for ballooning and 0-1 for inflammation.			

The ''safety population'' in the planned 18-month analysis of REGENERATE included 1,968 randomized patients who received at least one dose of investigational product (OCA or placebo).

Adverse events were generally mild to moderate in severity and the most common were consistent with the known profile of OCA. The frequency of serious adverse events was similar across treatment arms (11% in placebo, 11% in OCA 10 mg and 14% in OCA 25 mg) and no serious adverse event occurred in >1% of

patients in any treatment arm. There were 3 deaths in the study (2 in placebo: bone cancer and cardiac arrest, 1 in OCA 25 mg: glioblastoma) and none were considered related to treatment.

The most common adverse event reported was dose-related pruritus (19% in placebo, 28% in OCA 10 mg and 51% in OCA 25 mg). The large majority of pruritus events were mild to moderate, with severe pruritus occurring in a small number of patients (< 1% in placebo, < 1% in OCA 10 mg and 5% in OCA 25 mg). A higher incidence of pruritus associated treatment discontinuation was observed for OCA 25 mg (< 1% in placebo, < 1% in OCA 10 mg and 9% in OCA 25 mg). According to the clinical study protocol, investigator assessed severe pruritus mandated treatment discontinuation.

Consistent with observations from previous NASH studies, OCA treatment was associated with an increase in low density lipoprotein (''LDL'') cholesterol, with a peak increase of 22.6 mg/dL at four weeks and subsequently reversing and approaching baseline at month 18 (4.0 mg/dL increase from baseline). Triglycerides rapidly and continually decreased in the OCA treatment arms through month 18. There were few and varied serious cardiovascular events and incidence was balanced across the three treatment arms (2% in placebo, 1% in OCA 10 mg and 2% in OCA 25 mg).

With respect to hepatobiliary events, more patients (3%) on OCA 25 mg experienced gallstones or cholecystitis compared to < 1% on placebo and 1% on OCA 10 mg. While numerically higher in the OCA 25 mg treatment arm, serious hepatic adverse events were uncommon with < 1% incidence in each of the three treatment arms.

Phase 3 REVERSE Trial

We are currently conducting a Phase 3 clinical trial in NASH patients with compensated cirrhosis, known as the REVERSE trial. REVERSE is a randomized, double-blind, placebo-controlled, multicenter trial evaluating the safety and efficacy of OCA in histological improvement in fibrosis with no worsening of NASH in NASH patients with compensated cirrhosis. REVERSE is targeted to enroll approximately 540 patients with a biopsy-confirmed diagnosis of cirrhosis due to NASH.

The primary endpoint for REVERSE is the percentage of subjects with histological improvement in fibrosis by at least one stage with no worsening of NASH using the NASH Clinical Research Network scoring system after 12 months of treatment. Patients are randomized 1:1:1 into one of three treatment arms receiving a once-daily dose of placebo, OCA 10 mg or OCA 10 mg for the first three months with titration in accordance with the study protocol up to OCA 25 mg for the remaining nine months. Patients who successfully complete the double-blind phase of REVERSE will be eligible to enroll in an open-label extension phase for up to 12 additional months.

Phase 2 CONTROL Trial

In December 2015, we initiated a Phase 2 clinical trial, known as the CONTROL trial, to characterize the lipid metabolic effects of OCA and cholesterol management effects of concomitant statin administration in NASH patients. CONTROL enrolled approximately 80 NASH patients who were naïve to statin therapy or had undergone a statin washout period. Statin-naïve or washout patients were randomized to receive one of three doses of OCA (5 mg, 10 mg or 25 mg) or placebo. The study included a 16-week double-blind phase followed by an optional long-term safety extension (''LTSE'').

In July 2017, we announced that CONTROL met its primary objective by showing that newly initiated treatment with atorvastatin rapidly reversed OCA-associated increases in LDL cholesterol to below baseline levels. Most of the effect was observed four weeks after initiation of the lowest available dose of atorvastatin and was sustained throughout the study period. OCA treatment in the absence of statin therapy over the first four weeks resulted in an increase in LDL cholesterol across all OCA treatment groups, while the placebo group was relatively unchanged. Treatment with atorvastatin beginning at week four and continuing through week 16 reversed OCA-related increases in LDL cholesterol to below baseline levels in all OCA treatment groups. Dose-dependent pruritus was the most common adverse event in patients treated with OCA, occurring in 5% of patients on placebo, 5% of patients in the OCA 5 mg group, 10% of patients in the OCA 10 mg group and 55% of patients in the OCA 25 mg group. All adverse events were mild to moderate and two patients discontinued treatment in the OCA 25 mg group due to pruritus. Over 95% of the patients completing

the double-blind phase of CONTROL enrolled in the LTSE phase of the trial. During the LTSE phase of CONTROL, there was one patient death, which the principal investigator determined was unlikely related to OCA.

Phase 2 Sumitomo Dainippon Trial

In October 2015, we announced the results of a 72-week Phase 2 dose ranging trial of OCA in 200 adult patients with NASH in Japan. The trial was conducted by our collaborator, Sumitomo Dainippon Pharma Co., Ltd. (''Sumitomo Dainippon''). In this trial, 202 Japanese biopsy-proven NASH patients (NAS of 5-8) were randomized into one of four arms to receive either a 10 mg, 20 mg or 40 mg dose of OCA or placebo, and 200 of these patients (50 per group) initiated treatment for a 72-week double-blind treatment phase, followed by a 24-week off treatment phase. The primary endpoint was histologic improvement defined as at least a two-point improvement in NAS with no worsening of fibrosis.

The primary efficacy analysis was conducted on an ITT basis, testing the dose dependent effects of once daily OCA (10 mg, 20 mg and 40 mg) versus placebo on the primary endpoint. The ITT analysis included all randomized patients who received treatment (50 per group), and patients who discontinued or did not have a repeat biopsy were treated as non-responders. A pre-specified completer analysis was conducted on the patients who had biopsies at both baseline and 72 weeks (45, 44, 44 and 37 patients in the placebo, OCA 10 mg, OCA 20 mg and OCA 40 mg groups, respectively).

The Sumitomo Dainippon trial did not meet statistical significance for the primary endpoint. The ITT results in the table below show a dose dependent increase in the percentage of OCA-treated patients compared to placebo who achieved the primary endpoint (p = 0.053). Dose-dependent trends not reaching statistical significance were observed for several other pre-specified histologic endpoints, including the percentage of patients with steatosis and inflammation improvement, ballooning resolution and NASH resolution. No difference was seen in fibrosis improvement in the OCA groups compared to placebo.

ITT Results	**Placebo N = 50**	**OCA 10 mg N = 50**	**OCA 20 mg N = 50**	**OCA 40 mg N = 50**	
NAS improvement ≥ 2 points with no worsening of fibrosis	10 (20)%	11 (22)% p = 0.8070**	14 (28)% p = 0.3378**	19 (38)% p = 0.0496**	p = 0.053*

* Primary efficacy analysis is a stratified Cochran-Armitage test with multiple contrast coefficients. Statistical significance is based on a p-value < 0.05.

** The secondary efficacy analysis is a Cochran-Mantel-Haenszel (''CMH'') test stratified by baseline fibrosis stage for Pairwise comparison of each OCA group compared to the placebo group. The multiplicity was not adjusted.

In the completer analysis, similar dose dependent effects were observed, with 51% of patients in the OCA 40 mg dose group compared to 22% in the placebo group meeting the primary endpoint (p = 0.0061).

With the exception of dose dependent pruritus, OCA appeared to be generally safe and well tolerated. The number of pruritus associated discontinuations were 0, 0, 2 and 5 patients in the placebo, OCA 10 mg, OCA 20 mg and OCA 40 mg groups, respectively. Changes in lipid parameters, including LDL cholesterol, HDL cholesterol and triglycerides, appeared to be consistent with previously reported lipid changes in Western NASH patients. No other meaningful differences in the rate of adverse events between the OCA and placebo groups were noted.

Phase 2b FLINT Trial

In November 2014, the results from a Phase 2b clinical trial for the treatment of NASH, known as the FLINT trial, which was sponsored by the NIDDK, a part of the National Institutes of Health, were published in *The Lancet*. The FLINT trial was a double-blind, placebo-controlled trial of a once-daily dose of OCA 25 mg or placebo given for 72 weeks in 283 patients with biopsy-proven NASH. OCA achieved the primary endpoint in the FLINT trial, which was defined as an improvement of two or more points in NAS with no worsening of liver fibrosis.

The percentage of patients meeting the primary histological endpoint, based on liver biopsies, in the FLINT trial was 45% in the OCA treatment group and 21% in the placebo group ($p = 0.0002$, $n = 219$). The mean pre-treatment baseline NAS for patients in the OCA treatment group was 5.3 of a total possible score of eight (comprised of a NAS of 0-2 for hepatocellular ballooning, 0-3 for lobular inflammation and 0-3 for steatosis). Subgroup analyses showed significant response rates in the OCA treatment group in patients with risk factors for disease progression, including baseline fibrosis stage, co-morbid type 2 diabetes mellitus, ALT, insulin resistance and severe obesity (each factor $p < 0.05$ for OCA compared to placebo based on 95% confidence interval of published odds ratios).

A significantly greater number of OCA-treated patients also achieved the secondary endpoint of improvement of at least one fibrosis stage (35% versus 19%, $p = 0.004$), with OCA showing greater response rates as compared to placebo across all stages of fibrosis. Based on our retrospective analyses of the FLINT data, more OCA-treated patients exhibited fibrosis improvement of at least two fibrosis stages (15% versus 6%, not significant) and exhibited fibrosis improvements regardless of baseline fibrosis stage and a significantly greater number of OCA-treated patients also achieved complete resolution of fibrosis (17% versus 5%, $p = 0.0018$). Also, our retrospective analysis of the FLINT data showed that fewer OCA-treated patients progressed to bridging fibrosis (15% versus 18%, not significant) or to cirrhosis (2% versus 5%, not significant). Retrospective analyses after the un-blinding of results can potentially introduce bias and regulatory authorities typically give greatest weight to results from pre-specified analyses as compared to retrospective analyses. The NASH Clinical Research Network fibrosis staging system was used to categorize the pattern of fibrosis and architectural remodeling of the liver: no fibrosis (F0), perisinusoidal or periportal fibrosis (F1), perisinusoidal and periportal fibrosis (F2), bridging fibrosis (F3) and cirrhosis (F4). Fibrosis sub-stages 1a, 1b and 1c were considered F1 for the analysis.

The secondary endpoint of NASH resolution, based on a global histological assessment, also showed improvement, although not statistically significant (22% versus 13%, $p = 0.0832$). A central reading of all baseline and end-of-trial biopsies was performed at the end of the trial, based on which only 80% of patients were confirmed to have definite NASH, while the remaining 20% were diagnosed as borderline NASH (10%) or not-NASH (10%). A retrospective subgroup analysis on the completer population comprised only of definite NASH patients at baseline showed that a significantly greater number of OCA-treated patients achieved NASH resolution compared with placebo-treated patients (19% versus 8%; $p = 0.0278$).

In an additional retrospective analysis of data from the FLINT trial conducted in a REGENERATE-matched patient cohort published in 2018, (i) approximately 40% of OCA-treated patients as compared to approximately 21% of patients on placebo achieved at least a one-stage improvement in liver fibrosis without any worsening of NASH ($p = 0.02$) and (ii) approximately 20% of OCA-treated patients as compared to approximately 7% of patients on placebo achieved NASH resolution with no worsening of fibrosis ($p = 0.03$) using the definition we selected for NASH resolution in the REGENERATE trial.

In the FLINT trial, more OCA-treated patients experienced significant improvements in the major histological features of NASH, including steatosis (61% versus 38%, $p = 0.001$), lobular inflammation (53% versus 35%, $p = 0.006$) and hepatocellular ballooning (46% versus 31%, $p = 0.03$), as compared to the placebo treatment group. Trends were similar between the two treatment groups for portal inflammation, which is not a component of NAS and is typically mild in adult NASH patients.

The histological improvements observed in OCA-treated patients versus placebo were accompanied by statistically significant reductions in relevant biochemical parameters, including the serum liver enzymes ALT ($p < 0.0001$), aspartate aminotransferase (“AST”) ($p = 0.0001$) and gamma-glutamyl transferase (“GGT”) ($p < 0.0001$), each of which were above generally accepted normal limits at baseline, and total bilirubin ($p = 0.002$). A modest but statistically significant increase in ALP ($p < 0.0001$) in the OCA treatment group was also observed, but levels remained within typical normal limits.

OCA treatment was associated with serum lipid changes, including increases in total cholesterol and LDL cholesterol and a decrease in HDL cholesterol, that developed within 12 weeks of treatment initiation, then reversed through the end of treatment and returned to baseline during the 24-week post-treatment follow-up phase. Based on these observations, lipid management was emphasized partway into the trial, using accepted guidelines. At 72 weeks as compared to baseline, the following effects were observed in the OCA treatment

group: an increase in mean total cholesterol (0.16 mmol/L or 6 mg/dL increase OCA versus 0.19 mmol/L or 7mg/dL decrease placebo, p = 0.0009), an increase in mean LDL cholesterol (0.22 mmol/L or 9 mg/dL increase OCA versus 0.22 mmol/L or 8 mg/dL decrease placebo, p < 0.0001), a decrease in mean HDL cholesterol (0.02 mmol/L or 1 mg/dL decrease OCA versus 0.03 mmol/L or 1 mg/dL increase placebo, p = 0.01) and a decrease in triglycerides (0.22 mmol/L or 20 mg/dL decrease OCA versus 0.08 mmol/L or 7 mg/dL decrease placebo, p = 0.88, not significant). These changes in cholesterol levels, along with the achievement of pre-defined efficacy criteria, played a role in the decision of the FLINT data and safety monitoring board to terminate the treatment phase of the FLINT trial, and the publication of the FLINT results noted the need for further study of these changes.

A post-hoc analysis showed OCA-treated patients who initiated statins during the FLINT trial (n = 26) experienced a rapid reversal of their observed mean LDL cholesterol increase to below baseline levels, with a mean decrease after 72 weeks of treatment of -18.9 mg/dL. In contrast, other OCA-treated patients with no reported initiation or change in statin therapy experienced an increase in LDL cholesterol that peaked at week 12 and was sustained over the 72-week treatment period. Patients treated with statins at baseline who maintained statin treatment over the duration of the study (n = 50) experienced a mean LDL cholesterol increase of 8.7 mg/dL at 72 weeks. Patients not treated with statins during the study (n = 65) experienced a mean LDL cholesterol increase of 16.0 mg/dL. Treatment related LDL cholesterol increases in all groups reversed with treatment discontinuation. This analysis suggests that the OCA-associated LDL cholesterol increase reaches a maximum peak and plateaus soon after initiation of therapy and that concomitant statin use in NASH patients receiving OCA may mitigate treatment-related LDL cholesterol increases.

In the FLINT trial, statistically significant weight loss of an average of 2.3 kilograms was observed in OCA patients compared to no weight loss in the placebo group (p = 0.008), and this weight loss reverted towards baseline during the 24-week follow-up phase. A pre-specified sensitivity analysis conducted by the investigators showed that weight loss was not a driver of the primary endpoint. An increase in a marker of hepatic insulin resistance known as homoeostasis model assessment – estimated insulin resistance (‘‘HOMA-IR’’) (calculated using the product of fasting plasma insulin and glucose) was observed at 72 weeks in the OCA treatment group (p = 0.01). However, there was an imbalance in baseline plasma insulin levels (201 pmol/L OCA versus 138 pmol/L placebo), and an even larger relative and absolute increase in HOMA-IR was observed in the placebo group at the conclusion of the 24-week follow-up phase. This is potentially attributable to the inherent variability in HOMA-IR measurements, particularly in patients with type 2 diabetes, that have been shown to make single time-point to time-point changes of this magnitude clinically uninterpretable. There were virtually no changes in mean hemoglobin A1c, a measure of average blood sugar control over a period of approximately three months, in either OCA or placebo groups at 72 weeks. In a previous study of OCA in diabetic NAFLD patients, described in more detail below, employing the hyperinsulinemic-euglycemic insulin clamp, the gold standard for detecting changes in insulin resistance, OCA improved the glucose disposal rate consistent with reduced insulin resistance.

OCA was generally well tolerated in the FLINT trial. Adverse events were generally mild to moderate in severity and the incidence in the OCA and placebo treatment groups was similar for all symptoms except pruritus. Pruritus occurred more frequently in the OCA treatment group than in the placebo treatment group (23% vs. 6%, p < 0.0001) and at a higher grade (predominately moderate pruritus) but resulted in only one patient discontinuation. The incidence of severe or life-threatening events was not different between the two treatment groups and most of the events in both groups were deemed to be unrelated to treatment, including all severe or life-threatening cardiovascular events. There were two patient deaths in the Phase 2b FLINT trial, and neither death was considered related to OCA treatment.

Phase 2 Trial in Type 2 Diabetic Patients with NAFLD

In 2009, we announced the completion of a double-blind, placebo-controlled Phase 2 clinical trial of OCA in 64 type 2 diabetic patients with NAFLD. In this trial, OCA therapy significantly improved insulin sensitivity both in the liver and peripheral tissues, thereby meeting the primary endpoint in the trial with a mean improvement in liver insulin sensitization from baseline of approximately 24.5% in the combined OCA dose groups, as compared to a worsening of approximately 5.5% in the placebo group (p = 0.011). Insulin resistance, particularly in the liver, is considered to be an important contributor to NASH disease pathology. In this trial, significant reductions in body weight were also noted in patients receiving OCA therapy, along

with improvements in liver enzymes such as GGT and AST. OCA was generally well-tolerated by the trial patients, with side effects in the treatment groups not meaningfully different than those reported on placebo (apart from mild constipation in the OCA 50 mg group). Consistent with anticipated FXR-related lipid metabolic effects starting with the clearance of excess lipid load from the liver, there were changes in mean serum lipid profiles observed in the OCA treatment groups compared with the placebo group that included decreased concentrations of triglycerides, increased concentrations of LDL cholesterol and slightly decreased concentrations of HDL cholesterol from baseline. In our publication of the results, we observed that once-daily treatment for six weeks at the OCA 25 mg dose, which we subsequently selected to advance in our NASH development program, led to an approximately 12% decrease in mean triglycerides to 170 mg/dL from a baseline mean level of 193 mg/dL, an approximately 22% increase in mean LDL cholesterol to 120 mg/dL from a baseline mean level of 98 mg/dL, and an approximately 5% decrease in mean HDL cholesterol to 35 mg/dL from a baseline mean level of 37 mg/dL.

OCA for PSC

PSC is a rare, serious, chronic cholestatic liver disease characterized by a progressive, autoimmune-based destruction of bile ducts with eventual onset of cirrhosis. PSC is usually diagnosed by preliminary assessment of liver biochemistry, with or without reported symptoms, and confirmed by cholangiography. ALP is elevated in most PSC patients, consistent with cholestasis, and ALT and GGT are also typically elevated, but not in all cases. Bilirubin is often normal in early-stage PSC but increases with progression of the disease. The mean age at diagnosis is approximately 40 years. Approximately 75% of PSC patients have overlapping inflammatory bowel disease, principally ulcerative colitis. Median survival for PSC patients has been estimated to be 10 to 12 years from diagnosis in symptomatic patients, depending upon 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 is often complicated by the development of malignancies, with cholangiocarcinoma being the most common. Despite evaluation of multiple investigational treatments, there are no approved drugs for the treatment of PSC and liver transplant is currently the only treatment shown to improve clinical outcomes. However, the post-transplant recurrence rate of PSC has been shown to be as high as 20%. While UDCA is often prescribed off-label for the treatment of PSC due to improvements in liver biochemistry following initiation of therapy, it has not been shown to improve transplant-free survival and, at high doses, has been associated with increased risk for serious complications.

In 2017, we announced results from an international Phase 2 clinical trial, known as the AESOP trial, to evaluate the effects of 24 weeks of treatment with varying doses of OCA compared to placebo in patients with PSC. Patients were randomized to one of three treatment groups: placebo, OCA 1.5 mg to 3 mg and OCA 5 mg to 10 mg (with dose titration occurring at the 12-week midpoint). The primary endpoint was the reduction of serum ALP levels as compared to placebo for the OCA 5 mg to 10 mg group. In addition, OCA's effect on other secondary liver function endpoints, as well as symptoms of ulcerative colitis (a disease occurring in the majority of patients with PSC) was assessed. OCA achieved the primary endpoint of the AESOP trial: patients receiving OCA 5 mg daily with the option to titrate to 10 mg achieved a statistically significant reduction in ALP as compared to placebo at week 24 ($p < 0.05$). Patients in the OCA 1.5 mg to 3 mg group achieved statistically significant reductions in ALP versus placebo as measured by least square (''LS'') mean percent change from baseline at week 24. By week 24, ALP increased 1% in the placebo group and decreased by 22% in both the OCA 1.5 mg to 3 mg group ($p < 0.05$) and the OCA 5 mg to 10 mg group ($p < 0.05$).

A significant proportion of patients in the AESOP trial used UDCA, with 48%, 48% and 46% of patients on placebo, OCA 1.5 mg to 3 mg and OCA 5 mg to 10 mg, respectively, receiving UDCA at baseline. In a post-hoc analysis examining the effects of OCA in the presence and absence of UDCA, ALP reductions were observed with OCA regardless of treatment with UDCA. Patients receiving OCA monotherapy had greater reductions in ALP at week 12 and at week 24 as compared to patients who received OCA in addition to UDCA. At week 12, patients in the OCA 5 mg to 10 mg group receiving OCA monotherapy achieved a 30% LS mean reduction in ALP as compared to a 16% reduction in patients receiving OCA in combination with UDCA. At week 24, LS mean reductions in ALP in the OCA 5 mg to 10 mg group were 25% for patients receiving OCA monotherapy and 14% for patients receiving OCA in combination with UDCA.

Pruritus is a common symptom of PSC and was the most common adverse event, occurring in 46% of patients on placebo, 60% of patients in the OCA 1.5 mg to 3 mg group and 67% of patients in the OCA 5 mg to 10 mg group. One (4%) patient in the OCA 1.5 mg to 3 mg group and three (12%) patients in the OCA 5 mg to 10 mg group discontinued OCA due to pruritus compared to none in the placebo group. Following the completion of the 24-week double-blind portion of the trial, patients were given the option to enroll in an open-label, long-term safety and efficacy extension trial. Of those patients who completed the double-blind phase of the AESOP trial, 97% chose to participate in the open-label extension phase.

We believe that the results of the AESOP trial establish a proof-of-concept of OCA in a second cholestatic liver disease, are evaluating OCA for further development in PSC and continue to work with the FDA to define the regulatory path for approval in this rare but serious disease.

OCA for Biliary Atresia

Biliary atresia is a life-threatening condition in infants in which the bile ducts inside or outside the liver do not have normal openings. With biliary atresia, bile becomes trapped, builds up and damages the liver. The damage leads to scarring, loss of liver tissue, and cirrhosis. The two types of biliary atresia are fetal and perinatal. Fetal biliary atresia appears while the baby is in the womb. Perinatal biliary atresia is much more common and does not become evident until two to four weeks after birth. Some infants, particularly those with the fetal form, also have birth defects in the heart, spleen, or intestines. Biliary atresia is rare and only affects about one out of every 18,000 infants. The disease is more common in females, premature babies and children of Asian or African American heritage. Biliary atresia is not an inherited disease and is most likely caused by an event in the womb or around the time of birth. No single test can definitively diagnose biliary atresia, resulting in the need for a series of tests. All infants who still have jaundice two to three weeks after birth, or who have gray or white stools after two weeks of birth, should be checked for liver damage. Once diagnosed, biliary atresia is treated with a liver transplant or, more frequently, a surgery called the Kasai procedure, in which the bile ducts are connected directly to the small intestine. After the Kasai procedure, some infants continue to have liver problems and, even with the return of bile flow, some infants develop cirrhosis. Possible complications after the Kasai procedure include ascites, bacterial cholangitis, portal hypertension and pruritus. Even after a successful Kasai surgery, most infants with biliary atresia slowly develop cirrhosis over the years and require a liver transplant by adulthood.

In October 2015, we initiated a Phase 2 clinical trial of OCA in pediatric patients with biliary atresia, known as the CARE trial. The CARE trial is designed to evaluate the effects of 11 weeks of OCA treatment where patients with biliary atresia are randomized to varying doses of OCA. The primary endpoint is to evaluate the pharmacokinetics and the safety and tolerability of OCA treatment. In addition, OCA's effect on hepatobiliary indices and biomarkers will be assessed. This trial is targeted to enroll approximately 60 patients in the United States and Europe. In addition to studying the effects of OCA treatment in biliary atresia, we are undertaking the CARE trial as a part of an EMA-approved Pediatric Investigation Plan (''PIP'') supporting the conditional approval of Ocaliva for PBC in the European Union as PBC is not believed to occur in the pediatric population.

OCA and Bezafibrate

In December 2018, we entered into the Aralez Agreement, pursuant to which we acquired (i) Aralez's license to develop and commercialize bezafibrate in the United States (as amended and restated in connection therewith, the ''Bezafibrate License''), (ii) Aralez's IND on file with the FDA and other associated regulatory documentation and (iii) a non-exclusive license to certain of Aralez's intellectual property. Pursuant to the Aralez Agreement, we paid $9.0 million to Aralez in connection with the closing of the transactions contemplated thereby in December 2018 and are obligated to make a $2.0 million milestone payment to Aralez based on the occurrence of specified regulatory-related events. Bezafibrate, a PPAR agonist that has been studied in PBC, is not approved in the U.S. for any indication. We intend to evaluate the efficacy, safety and tolerability of bezafibrate in combination with OCA in patients with PBC in a Phase 2 study, with the longer-term goal of developing and seeking regulatory approval for a fixed dose combination regimen in this indication and potentially other liver diseases. Pursuant to the Bezafibrate License, we are also obligated to make a $2.5 million milestone payment based on the occurrence of specified regulatory-related events with respect to such a combination product, as well as mid-single digit percentage royalty payments based on the net sales of such a combination product.

Pipeline Compounds

We, together with our collaborators, have discovered other bile acid chemistry-based compounds that are in earlier stages of screening, research and development. Among these compounds are INT-767 and INT-787. INT-767 is an orally administered dual FXR and TGR5 agonist that, like OCA, is derived from the primary human bile acid chenodeoxycholic acid. TGR5 is a G-protein coupled bile acid receptor that has been shown to affect energy metabolism, glucose homeostasis, bile composition/secretion and inflammation. INT-767 appears to be a more potent FXR agonist than OCA and has shown potential anti-fibrotic and anti-inflammatory effects in animal models. We have also completed a Phase 1 clinical trial of INT-767, the goal of which was to assess safety and pharmacokinetics in a single ascending dose escalation phase followed by a multiple ascending dose phase in healthy volunteers. INT-787 is an FXR agonist that we are currently evaluating in preclinical studies. INT-787 appears to be a more selective FXR agonist than OCA and has shown potential anti-fibrotic and anti-inflammatory effects in animal models. In addition, we believe that bile acid chemistry may have utility in a broad range of diseases outside of our core area of focus and have in the past, and may in the future, explore the potential application of our development compounds in non-core areas.

Sumitomo Dainippon Collaboration

In March 2011, we entered into an exclusive license agreement (the ''Original Sumitomo Agreement'') with Sumitomo Dainippon, pursuant to which we granted to Sumitomo Dainippon an exclusive license to research, develop and commercialize OCA for the treatment of PBC and NASH in Japan and China (excluding Taiwan) and an option to research, develop and commercialize OCA in certain countries outside of such territories (the ''Country Option''). We received an upfront payment from Sumitomo Dainippon of $15.0 million under the terms of the Original Sumitomo Agreement. In May 2014, Sumitomo Dainippon exercised the Country Option in part to add Korea as part of its licensed territories and paid us a $1.0 million upfront fee in connection therewith. In February 2018, we and Sumitomo Dainippon entered into Amendment No. 3 (the ''Sumitomo Amendment'') to the Original Sumitomo Agreement (as amended, the ''Sumitomo Agreement''), pursuant to which (i) Sumitomo Dainippon agreed to return the rights to develop and commercialize OCA in Japan and Korea and waived its rights to the Country Option, (ii) we agreed to forego any further milestone or royalty payments relating to the development and commercialization of OCA in Japan and Korea and (iii) certain milestone payment obligations with respect to the development and commercialization of OCA were adjusted. In addition, we and Sumitomo Dainippon agreed that if certain clinical development milestones in China are not met by December 31, 2020, Sumitomo Dainippon may choose either to make a milestone payment to us or terminate the Sumitomo Agreement. Sumitomo Dainippon may also terminate the Sumitomo Agreement in its entirety or on an indication-by-indication basis at any time upon 90 days' written notice. As of December 31, 2018, we had achieved $6.0 million of development milestones under the Sumitomo Agreement. We may be eligible to receive additional milestone payments under the Sumitomo Agreement in an aggregate amount of up to approximately $23.0 million based on the occurrence of certain clinical trial and regulatory-related events and tiered royalty payments up to the mid-twenties in percentage terms based on net sales of OCA products in China (excluding Taiwan).

Competition

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We have competitors in the United States, Europe and other jurisdictions, including major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical and generic drug companies and universities and other research institutions. Many of our competitors have financial, sales and marketing, manufacturing and distribution, legal, regulatory and product development resources substantially greater than ours. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies.

The ability of Ocaliva for PBC, OCA for NASH, if approved, and other future approved products, if any, to compete with products sold by other companies will depend on a number of factors, including efficacy, safety and tolerability, reliability, convenience of dosing, price, the level of branded and generic competition and reimbursement. We believe that the competitive environment for Ocaliva for PBC and, if approved, OCA for NASH is as follows.

Ocaliva for PBC

Ocaliva competes with UDCA (or ursodiol), a first-line therapy approved for the treatment of PBC that is available generically at a significantly lower cost than Ocaliva. Ocaliva is an FXR agonist and we are aware of several other companies that have FXR agonists in Phase 2 or earlier clinical or preclinical development for the treatment of PBC, including FXR agonists from Novartis AG (tropifexor), Gilead Sciences, Inc. (GS-9674) and Enanta Pharmaceuticals, Inc. (EDP-305). Additional product candidates in Phase 3 or earlier clinical or preclinical development for the treatment of PBC include Genfit SA's dual PPAR alpha/delta agonist (elafibranor), CymaBay Therapeutics, Inc.'s PPAR delta agonist (seladelpar), Arena Pharmaceuticals, Inc.'s S1P receptor modulator (etrasimod), Bristol-Myers Squibb Company's anti-CTL4 fusion protein (abatacept) and Fast Forward Pharmaceuticals BV's anti-CD40 monoclonal antibody (FFP104). Additionally, several companies have product candidates aimed at the cholestatic-induced pruritus associated with PBC, including apical sodium dependent bile acid transport inhibitors being developed by GlaxoSmithKline plc (GSK2330672).

Off-label uses of other potential treatments may also compete with Ocaliva for PBC. For example, while fibrates are not approved for use in PBC, off-label use of fibrate drugs has been reported. Bezafibrate, a fibrate that is not approved by the FDA for any indication and is only available outside of the United States, has been studied in PBC.

OCA for NASH

There are currently no medications approved for the treatment of NASH. However, various therapeutics are used off-label for the treatment of NASH, including vitamin E (an antioxidant), insulin sensitizers (e.g., metformin, pioglitazone), antihyperlipidemic agents (e.g., gemfibrozil), pentoxifylline and UDCA. There are several product candidates in Phase 3 or earlier clinical or preclinical development for the treatment of NASH, including Genfit SA's PPAR alpha/delta agonist (elafibranor), Gilead Sciences, Inc.'s ASK-1 inhibitor (selonsertib) and Allergan plc's dual CCR2 and CCR5 inhibitor (cenicriviroc), as well as FXR agonists from Novartis AG (tropifexor), Gilead Sciences, Inc. (GS-9674) and Enanta Pharmaceuticals, Inc. (EDP-305).

Additional pharmaceutical and biotechnology companies with product candidates in development for the treatment of NASH include AstraZeneca plc, Boehringer Ingelheim GmbH, Bristol-Myers Squibb Company, Conatus Pharmaceuticals Inc., CymaBay Therapeutics, Inc., Durect Corporation, Galectin Therapeutics Inc., Galmed Pharmaceuticals Ltd., Immuron Ltd., Ionis Pharmaceuticals, Inc., Islet Sciences, Inc., Madrigal Pharmaceuticals, Inc., MediciNova, Inc., MiNA Therapeutics, NGM Biopharmaceuticals, Inc., Novo Nordisk A/S, NuSirt Sciences Inc., Viking Therapeutics, Inc. and Zydus Pharmaceuticals (USA) Inc. NASH is a complex disease and we believe that it is unlikely that any one therapeutic option will be optimal for every NASH patient.

In addition, many universities and private and public research institutions may become active in our target disease areas. The results from our clinical trials and the approval of Ocaliva for PBC have brought more attention to our targeted indications and bile acid chemistry. As a result, we believe that additional companies and organizations may seek to compete with us in the future. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis technologies and drug products that are more effective or less costly than OCA or any other product candidates that we are currently developing or that we may develop, which could render our products or product candidates obsolete and noncompetitive. Our ability to compete may also be affected because, in many cases, insurers or other third-party payors seek to encourage the use of generic products.

Intellectual Property

Protecting our intellectual property, such as our patents, is a key part of our strategy. We are the owner of record of numerous issued U.S. and non-U.S. patents with claims directed to pharmaceutical compounds, pharmaceutical compositions, methods of making these compounds and methods of using these compounds in various indications. In addition, we are the owner of record of numerous pending U.S. and non-U.S. patent applications, and regularly pursue additional patent applications in various jurisdictions. We also have numerous trademark and service mark registrations and pending trademark and service mark applications in the United States and abroad.

The patent portfolio for OCA contains U.S. and non-U.S. patents and patent applications directed to compositions of matter, methods of use and manufacturing methods. Our primary composition of matter patent for OCA expires in 2022. In light of the U.S. marketing approval of Ocaliva for PBC in May 2016, we have applied for an extension of the patent term for this patent in the United States through 2027. In addition, in connection with the conditional approval of Ocaliva for PBC in the European Union, we have applied for supplementary patent certification (''SPC'') to extend the patent term for this patent in the European Union through 2027. We have received grants of SPC in Austria, Denmark, France, Germany, Ireland, Italy, Norway, Spain and Sweden and we expect to take similar actions in other jurisdictions and countries where similar regulations exist.

The table set forth below summarizes the U.S. patents covering OCA that are listed in the FDA's Orange Book List of Approved Drug Products With Therapeutic Equivalence Evaluations (the ''Orange Book''). The issued composition of matter patents for OCA are expected to expire in 2022 at the earliest and 2036 at the latest if the appropriate maintenance, renewal, annuity, or other government fees are paid. We expect that the other patents in the OCA portfolio that are listed in the Orange Book would expire as set forth below, assuming the appropriate maintenance, renewal, annuity or other governmental fees are paid.

Patent No.	Type of Patent[1]	Brief Summary of Patent	U.S. Patent Expiration
7,138,390	Composition of Matter	Claims OCA compound	2022[2]
8,058,267	Method of Use	Claims methods of treating PBC with OCA	2022
8,377,916	Method of Use	Claims methods of treating PBC with OCA	2022
9,238,673	Composition of Matter	Claims OCA active pharmaceutical ingredient (''API'')	2033
10,047,117	Method of Use	Claims methods of treating FXR mediated diseases with OCA API	2033
10,052,337	Composition of Matter	Claims OCA finished drug product	2036
10,174,073	Composition of Matter	Claims OCA API produced by a specified process	2033

(1) You should read the risk factors included elsewhere in this Annual Report on Form 10-K for important information about risks posed by the loss of patent protection, in particular the risks described under ''Risk Factors — Risks Related to Our Intellectual Property.''

(2) In light of the U.S. marketing approval of Ocaliva for PBC in May 2016, we have applied for an extension of the patent term for this patent in the United States through 2027.

In addition, we have intellectual property protecting OCA that we would expect to list in the Orange Book if OCA is approved for the treatment of NASH.

We may 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 to protect our trade secrets and other proprietary information. We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems.

Our commercial success will depend in part on our ability to obtain and maintain patent, trademark and trade secret protection covering our products such as Ocaliva and product candidates, as well as our ability to successfully defend our intellectual property against third-party challenges. Our ability to stop third parties from making, using, selling, offering to sell or importing our products is dependent upon the extent to which we have regulatory exclusivity or intellectual property-based exclusivity rights under valid and enforceable patents or other intellectual property that cover our products. If we fail to obtain and maintain adequate intellectual property protection, we may not be able to prevent third parties from launching generic versions of our products, from using our proprietary technologies or from marketing products that are very similar or identical to ours. The patent positions of 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 foreign jurisdictions, and the legal standards relating to the patentability, validity and enforceability of pharmaceutical patents are evolving.

Changes in either the patent laws or in interpretations of patent laws in U.S. and foreign jurisdictions may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be enforced in the patents that we currently own or that may issue from the applications we have filed or may file in the future or those that we may license from third parties. Additionally, our currently pending or future patent applications may not result in issued patents, and any term extensions that we seek may not be granted. Further, if any patents we obtain or license are deemed invalid or unenforceable, it could impact our ability to commercialize or license our technology or enable third parties to develop and market products that are similar or identical to ours.

Manufacturing and Supply

We do not own or operate manufacturing facilities for the production of Ocaliva, OCA or any of our other product candidates, and we do not have any plans to develop our own manufacturing operations in the foreseeable future. We rely on third-party contract manufacturers for all of our required raw materials, API and finished product for our commercial sales and for our clinical trials and preclinical studies.

We currently have an agreement with PharmaZell GmbH (“PharmaZell”) for the manufacture and commercial supply of Ocaliva. Pursuant to our agreement with PharmaZell, we are obligated during the term of the agreement to purchase from PharmaZell a certain percentage of our annual commercial requirements of API for use in Ocaliva and, if approved, OCA for NASH or other indications. The initial term of our agreement with PharmaZell expires on December 31, 2020 and thereafter automatically renews for successive two-year periods unless either party provides notice of non-renewal at least 12 months prior to the end of the initial term or then-current renewal term. The agreement is also subject to customary early termination rights.

We have engaged in activities to qualify additional or back-up suppliers, but these suppliers may not be able to meet our long-term commercial supply requirements for Ocaliva or, if approved, OCA for NASH or other indications on acceptable terms, or at all. We do not have agreements for long-term supplies of any of our other product candidates. We currently obtain supplies and services relating to our other product candidates from our third-party contract manufacturers on a purchase order basis

Contract manufacturers are subject to extensive governmental regulation and we depend on them for compliance with the requirements of U.S. and non-U.S. regulators for the manufacture of our finished products, including Ocaliva. We intend to continue to rely on third-party manufacturers for the manufacture of Ocaliva, OCA for NASH, if approved, other future approved products, if any, and our clinical-stage product candidates. We believe this manufacturing strategy will enable us to direct financial resources to the development and commercialization of products rather than diverting resources to establishing a manufacturing infrastructure. See “Risk Factors — Risks Related to Our Dependence on Third Parties — We rely entirely on third parties for the manufacture of our product requirements for our preclinical studies and clinical trials, as well as our commercial supply of Ocaliva and, if approved, OCA for NASH and our other product candidates, and also depend on third-party vendors and CROs for certain of our clinical trial and product development activities. Our business could be harmed if our third-party manufacturers fail to provide us with sufficient quantities of drug product, or fail to do so at acceptable quality levels or prices, or we lose our relationships with our third-party vendors and CROs and our clinical trial or product development efforts are delayed as a result.”

Sales and Marketing

Ocaliva is our first approved product and the commercial launch of Ocaliva for PBC is our first product launch. We are commercializing Ocaliva for PBC using a combination of our internal commercial organization, a contract sales organization and third-party distributors depending on the jurisdiction. In addition, Sumitomo Dainippon has an exclusive license to develop and commercialize OCA for the treatment of PBC and NASH in China (excluding Taiwan). We are developing our commercialization strategy for OCA for NASH, if approved, and have not yet decided on our commercialization strategy for OCA for other indications or for our other product candidates, in each case, if approved. We intend to continue to evaluate how best to commercialize our product candidates, if approved, in the United States and internationally, and

may choose to collaborate with third parties that have sales and marketing capabilities and established distribution systems, either to augment our own capabilities or in lieu thereof.

Customers

We commenced our commercial launch of Ocaliva for the treatment of PBC in the United States in June 2016. In December 2016, the European Commission granted conditional approval for Ocaliva for the treatment of PBC and we commenced our European commercial launch in January 2017. Since January 2017, Ocaliva has also received regulatory approval in several of our target markets outside the United States and Europe, including Canada, Israel and Australia. We recognized net sales of Ocaliva of $177.8 million, $129.2 million and $18.2 million for the years ended December 31, 2018, 2017 and 2016, respectively. We sell Ocaliva to a limited number of specialty pharmacies which dispense the product directly to patients. The specialty pharmacies are referred to as our customers. For a discussion of our customer concentration, see Note 2 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and analogous authorities in other countries extensively regulate, among other things, the research, development, testing, manufacture, labeling, packaging, promotion, storage, advertising, distribution, marketing and export and import of products such as Ocaliva and those we are developing. Our product candidates must be approved by the FDA through the NDA process before they may be legally marketed in the United States and by the European Commission following a favorable assessment provided by the EMA through the MAA process for a product falling within the scope of the Centralized procedure or a national MAA process (albeit through the process of Mutual Recognition or Decentralized procedure) before they may be legally marketed in the European Union. Our product candidates will be subject to similar requirements in other countries prior to marketing in those countries. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

United States Government Regulation

NDA Approval Processes

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, as amended (the ‘‘FDCA’’) and implementing regulations. An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA’s good laboratory practice regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board (‘‘IRB’’), representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices (‘‘GCP’’) to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of an NDA;
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices (‘‘cGMP’’) requirements and to assure that the facilities, methods and controls are adequate to preserve the product’s identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCP and the integrity of the clinical data;

- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including, as applicable, Risk Evaluation and Mitigation Strategies (‘‘REMS’’) and post-approval studies required by the FDA.

Preclinical and Clinical Studies

Once a pharmaceutical candidate is identified for development, it enters the preclinical or nonclinical testing stage. Nonclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the nonclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. Some nonclinical testing may continue even after the IND is submitted. In order to conduct clinical research, we must submit an IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, or any time thereafter, places the IND on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin or continue. A clinical hold may affect one or more specific studies or all studies conducted under the IND.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCPs. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, research subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and progress reports detailing the status of the clinical trials must be submitted to the FDA annually. Sponsors also must timely report to the FDA serious and unexpected adverse reactions, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigation brochure, or any findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug. An IRB must review and approve the protocol before a clinical trial commences at each institution and must also approve the information regarding the trial and the consent form that must be provided to each research subject or the subject’s legal representative, monitor the study until completed and otherwise comply with IRB regulations.

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 elimination. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be inherently too toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- *Phase 2.* Clinical trials are performed on a limited patient population intended to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- *Phase 3.* Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population generally at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product and provide an adequate basis for product labeling.

Human clinical trials are inherently uncertain and Phase 1, Phase 2 and Phase 3 testing may not be successfully completed. The FDA or the sponsor may suspend a clinical trial at any time for a variety of reasons, 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. In some cases, clinical trials are overseen by an independent group of qualified experts organized by the trial sponsor, or the clinical monitoring board or data safety monitoring board (‘‘DSMB’’). This group provides authorization for whether or not a trial may move forward at designated check points. These decisions are based on the DSMB’s independent review of the limited access to data from the ongoing trial.

Sponsors of clinical trials of certain FDA-regulated products, including prescription drugs, are required to register and disclose clinical trial information related to the product, patient population, phase of investigation, clinical trial sites and investigator, and other aspects of the clinical trial on a public website maintained by the U.S. National Institutes of Health. Sponsors are also obligated to disclose the results of these clinical trials after completion. For a new product or a new indication for a previously approved product, sponsors can delay submission of clinical study results for up to two years until the product has been approved or approved for the new use. Competitors may use this publicly-available information to gain knowledge regarding the design and progress of our development programs.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to the submission of an IND, at the end of Phase 2 and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date and for the FDA to provide advice on the next phase of development. Sponsors typically use the meeting at the end of Phase 2 to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial that they believe will support the approval of the new drug. If a Phase 2 clinical trial is the subject of discussion at the end of Phase 2 meeting with the FDA, a sponsor may be able to request a special protocol assessment (''SPA''), the purpose of which is to reach agreement with the FDA on the Phase 3 clinical trial protocol design and analysis that will form the primary basis of an efficacy claim.

According to published guidance on the SPA process, a sponsor which meets the prerequisites may make a specific request for an SPA and provide information regarding the design and size of the proposed clinical trial. The FDA is supposed to evaluate the protocol within 45 days of the request to assess whether the proposed trial is adequate, and that evaluation may result in discussions and a request for additional information. An SPA request must be made before the proposed trial begins, and all open issues must be resolved before the trial begins. If a written agreement is reached, it will be documented and made part of the record. The agreement is generally expected to be binding on the FDA, in that the critical design elements agreed to as part of an SPA agreement may not be changed by the sponsor or the FDA after the trial begins except with the written agreement of the sponsor and the FDA or if the FDA determines that a substantial scientific issue essential to determining the safety or efficacy of the drug was identified after the testing began. The presence of an SPA agreement does not guarantee that a marketing application will be filed or approved, even if the trial is conducted in accordance with the protocol. In rare cases, FDA may rescind an SPA agreement.

Concurrent with clinical trials, sponsors usually complete additional animal safety studies and also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing commercial quantities of the product in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug and the manufacturer must develop methods for testing the quality, purity and potency of the drug prior to release. 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 proposed shelf-life.

The results of product development, nonclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests and other control mechanisms, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of user fees, but a waiver of such fees may be obtained under specified circumstances. Currently, the application fee is approximately $2.6 million for NDAs with clinical data and approximately $1.3 million for NDAs without clinical data. The sponsor under an approved NDA is also subject to annual program user fees, currently $309,915. Program fees are assessed for each approved prescription drug product identified in an approved application, up to five program fees per application. These fees are typically modified annually. The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. It may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

Once the submission is accepted for filing, the FDA begins an in-depth review. NDAs receive either standard or priority review. A drug representing a significant improvement over available therapies in treatment, prevention or diagnosis of disease may receive priority review. The FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data. Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. The FDA reviews an NDA to determine, among other things, whether a product is safe, effective, and can be properly manufactured for its intended use or uses. The FDA may refer the NDA to an advisory committee for review and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured and tested.

Fast Track, Breakthrough Therapy, Priority Review and Accelerated Approval

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs include fast track designation, breakthrough therapy designation and priority review designation.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track designated products, sponsors may have a higher number of interactions with the FDA and the FDA may initiate review of sections of a fast track product's NDA before the application is complete.

A product may also be designated as a breakthrough therapy if it is intended, either 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 product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner. In January 2015, OCA received breakthrough therapy designation from the FDA for the treatment of NASH patients with liver fibrosis.

The FDA may also designate a product for priority review if it is a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. Certain other applications may also qualify for priority review. The FDA determines, on a case-by-case basis, whether the proposed drug represents a significant improvement when compared with other available therapies. A priority designation by the FDA is intended to direct the agency's attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

In addition, the FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, and 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. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval. In the case of unprecedented accelerated approval endpoints, this determination occurs during the review of the NDA. Unless otherwise informed by the FDA, an applicant must submit to the FDA for consideration during the preapproval review period copies of all promotional materials, including promotional labeling as well as advertisements, intended for dissemination or publication within 120 days following marketing approval. After 120 days following

marketing approval, unless otherwise informed by the FDA, the applicant must submit promotional materials at least 30 days prior to the intended time of initial dissemination of the labeling or initial publication of the advertisement.

As a condition of a grant of accelerated approval, the FDA may require that the sponsor perform one or more controlled post-marketing clinical trials. Approval of a drug may be withdrawn if these trials fail to verify clinical benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the drug (e.g., show a significantly smaller magnitude or duration of benefit than was anticipated based on the observed effect on the surrogate).

Ocaliva was granted fast track designation by the FDA for the treatment of patients with PBC who have an inadequate response to or are intolerant of UDCA. In August 2015, the FDA accepted for review our NDA and granted priority review for Ocaliva in PBC. On May 27, 2016, Ocaliva was approved under the accelerated approval pathway in the United States for PBC in combination with UDCA in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA.

Post-approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in new labeling information (e.g., warnings), customer training and/or education requirements, restrictions on the product or even complete withdrawal of the product from the market. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further FDA review and approval. In addition, the FDA may require studies, trials, analyses, and surveillance programs to monitor or evaluate the effect of approved products that have been commercialized, and the FDA has the power to limit further marketing of a product, or seek withdrawal of approval, based on the results of these post-marketing programs.

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 some state agencies for compliance with cGMP and other laws. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Failure to comply with the applicable U.S. requirements at any time during the product development process or approval process, or after approval, may subject us to regulatory or statutory sanctions, any of which could have a material adverse effect on us.

These sanctions could include:

- refusal to approve pending applications;
- withdrawal of an approval;
- imposition of a clinical hold;
- warning or untitled letters;
- product seizures;
- total or partial suspension of production or distribution; or
- injunctions, fines, disgorgement, or civil or criminal penalties.

The FDA and other US state and federal authorities regulate marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in a manner otherwise consistent with the provisions of the approved label. The FDA and other authorities actively enforce the laws and regulations prohibiting false, misleading, deceptive, or off-label promotional practices; violations of these prohibitions can lead to significant liability. Additional regulations apply for advertising and promotion of products approved under the accelerated approval pathway. Unless otherwise informed by the FDA, an applicant must submit to the FDA for consideration during the preapproval review period copies of all promotional materials, including promotional labeling as well as advertisements, intended for dissemination or publication within 120 days following marketing approval. After 120 days following marketing approval, unless otherwise informed by the FDA, the applicant must submit promotional materials at least 30 days prior to the intended time of initial dissemination of the labeling or initial publication of the advertisement.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products. Future FDA and state inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct.

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. In addition, FDA regulations and guidance are often revised or reinterpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether legislative changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

In accordance with the applicable requirements under the accelerated approval pathway, we initiated our Phase 4 COBALT clinical outcomes confirmatory trial for Ocaliva in PBC in December 2014, following discussions with the FDA. COBALT will be completed on a post-marketing basis. The study evaluates subjects across the spectrum of PBC disease, including early and advanced PBC. We have agreed to evaluate the safety and efficacy of Ocaliva in patients with moderate to severe hepatic impairment and as monotherapy in patients with PBC. In addition, we have agreed to develop and characterize a lower dose formulation of Ocaliva to allow for once daily dosing in patients with moderate or advanced hepatic impairment.

Risk Evaluation and Mitigation Strategy

The Food and Drug Administration Amendments Act of 2007 created a new section of the FDCA which authorizes the FDA to require a REMS when necessary to ensure that the benefits of a drug outweigh the risks. Under a REMS, the FDA may require various measures to address serious risks, such as training or registries, as well as steps to monitor and assess the effectiveness of those measures. Such requirements may impose significant burdens on prescribers, pharmacists or patients.

We do not have a REMS for Ocaliva for the treatment of PBC.

Patent Term Extension and Data Exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use of our drug candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 (the ‘‘Hatch-Waxman Act’’). The Hatch-Waxman Act permits an extension of a patent term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, the extension of patent term cannot extend the remaining term of a patent beyond a total of 14 years from the product’s approval date. The patent term extension 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 extension must be made prior to expiration of the patent. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. Our primary composition of matter patent for OCA expires in 2022. In light of the U.S. marketing approval of Ocaliva for PBC in May 2016, we have applied for an extension of the patent term for this patent in the United States through 2027. In addition, in connection with the conditional approval of Ocaliva for PBC in the European

Union, we have applied for SPC to extend the patent term for this patent in the European Union through 2027. We have received grants of SPC in Austria, Denmark, France, Germany, Ireland, Italy, Norway, Spain and Sweden and we expect to take similar actions in other jurisdictions and countries where similar regulations exist. In the future, we intend to apply for restorations of patent term for some of our currently owned or licensed patents to add patent life beyond their current expiration date, depending on the expected length of clinical trials and other factors involved in the submission of the relevant NDA.

Data exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain 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 as further defined in FDA regulations. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application (''ANDA'') or a 505(b)(2) NDA for a drug with the same active moiety. However, an application may be submitted after four years if it contains a paragraph IV certification that a reference product patent is invalid or not infringed by the ANDA or 505(b)(2) product. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an approved 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, for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the original active moiety for other conditions 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.

Pediatric Exclusivity and Pediatric Use

Under the Best Pharmaceuticals for Children Act, certain drugs may obtain an additional six month extension to existing unexpired regulatory exclusivities and listed patents, if the sponsor submits information that responds to a written request by FDA and that and are conducted in accordance with applicable scientific principles and protocols. We have not received such a written request from FDA for such pediatric studies, although we may ask the FDA to issue a Written Request for such studies in the future.

In addition, under the Pediatric Research Equity Act (the ''PREA''), an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless the sponsor receives a deferral or waiver. However, FDA has recently issued guidance limiting a sponsor's ability to waive the PREA study requirements.

Orphan Drug Designation

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

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any applications from any other party to market the same drug for the same indication for seven years, except in very limited circumstances such as where there is a demonstration of clinical superiority. Orphan drug exclusivity, however, could also work to block the approval of one of our products for seven years if a competitor is first to market for an orphan indication for a drug considered the same drug as one of our drug candidates and obtains approval and orphan exclusivity for the same indication or disease

for which our candidate is being developed. Orphan drug exclusivity would not block approval of a competitor's same drug for a use different from the orphan-protected use and would not block approval of a competitor drug considered a different drug for any indication, including the orphan-protected use. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to orphan exclusivity for the full scope of its approved use.

As in the United States, we may apply for designation of a product as an orphan drug for the treatment of a specific indication in the European Union before the application for marketing authorization is made. Orphan drugs in Europe enjoy economic and marketing benefits, including up to ten years of market exclusivity for the approved indication. The market exclusivity period for the authorized therapeutic indication may be reduced to six years if, at the end of the fifth year, it is established that the orphan designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. In addition, a competing similar medicinal product may in limited circumstances be authorized prior to the expiration of the market exclusivity period, including if it is shown to be safer, more effective or otherwise clinically superior to the orphan-designated product.

OCA has received orphan drug designation in the United States and the European Union for the treatment of PBC and PSC. In the United States, Ocaliva has also received orphan exclusivity for its approved PBC indication that runs until May 27, 2023.

Regulation Outside of the United States

In addition to regulations in the United States, we will be subject to regulations of other countries governing clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of countries outside of the United States before we can commence clinical trials in such countries and approval of the regulators of such countries or economic areas, such as the European Union, before we may market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Under European Union regulatory systems, a company may submit marketing authorization applications under the centralized, decentralized or mutual recognition marketing authorization procedure. The centralized procedure provides for the grant of a single marketing authorization for a medicinal product by the European Commission on the basis of an opinion provided by the EMA's Committee for Medicinal Products for Human Use (the "CHMP"). A centralized marketing authorization is valid for all European Union member states and the European Economic Area States (Iceland, Liechtenstein and Norway). The decentralized marketing authorization procedure involves the submission of an application for marketing authorization to the competent authorities in each of the European Union member states chosen by the applicant in which the product is to be marketed. One national competent authority, selected by the applicant (Reference Member State) leads the assessment of the application for marketing authorization. The competent authorities of the other chosen European Union member states concerned by the procedure (Concerned Member States) are subsequently required to review the initial evaluation and, if the assessment is positive and all issues are resolved, grant marketing authorization for their territory on the basis of this assessment, except where grounds of potential serious risk to public health require this application for authorization to be refused. The mutual recognition procedure provides for mutual recognition of a marketing authorization which has already been granted by the national competent authority of a European Union member state by the competent authorities of the other European Union member states where further marketing authorizations are progressively sought. The holder of a national marketing authorization may submit an application to the competent authority of a European Union member state requesting that this authority recognize the marketing authorization granted by the competent authority of another European Union member state.

Prior to obtaining a marketing authorization in the European Union submitted as a full stand-alone dossier, applicants have to demonstrate compliance with all measures included in an EMA-approved PIP covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver, or (3) a deferral for one or more of the measures included in the PIP. In the case of orphan

medicinal products, completion of an approved PIP can result in an extension of the aforementioned market exclusivity period from ten to twelve years.

It is also possible that a centralized marketing authorization could be conditional on post-approval studies and not considered a full approval, but subject to annual renewal until comprehensive data are provided to confirm the benefit/risk assessment. A manufacturer's ability to obtain and maintain conditional marketing authorization in the European Union will be limited to specific circumstances and subject to several conditions and obligations, if obtained at all. Conditional marketing authorizations can be granted, based on a clinical dataset that is not comprehensive. Granting of such an authorization may be granted for a limited number of medicinal products for human use referenced in the applicable European Union law governing conditional marketing authorization, including products designated as orphan medicinal products under European Union law, if (1) the risk-benefit balance of the product is positive, (2) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (3) unmet medical needs will be fulfilled and (4) the benefit to public health of the immediate availability on the market of the medicinal product outweighs the risk inherent in the fact that additional data are still required. Specific obligations, including with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data, may be specified in the conditional marketing authorization. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions.

Similarly to the United States, both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual European Union member states both before and after grant of the manufacturing and marketing authorizations. This includes European Union GMP rules, which govern quality control of the manufacturing process and require documentation policies and procedures. We and our third-party manufacturers are required to ensure that all of our processes, methods, and equipment are compliant with GMP.

Failure by us or by any of our third-party partners, including suppliers, manufacturers, and distributors to comply with European Union laws and the related national laws of individual European Union member states governing the conduct of clinical trials, manufacturing approval, marketing authorization of medicinal products and manufacturing and marketing of such products, both before and after grant of marketing authorization, may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials or to grant marketing authorization, product withdrawals and recalls, product seizures, suspension, withdrawal, or variation of the marketing authorization, total or partial suspension of production, distribution, manufacturing, or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

In October 2016, the CHMP of the EMA adopted a positive opinion recommending the granting of a conditional marketing authorization of Ocaliva in PBC. Based on the CHMP's positive recommendation, the European Commission granted a conditional marketing authorization of Ocaliva in PBC in December 2016. PBC is not believed to occur in the pediatric population. Therefore, in accordance with applicable regulations, this marketing authorization required demonstration of compliance with all measures included in an EMA-approved Pediatric Investigation Plan for OCA for the treatment of biliary atresia, a pediatric cholestatic disease.

Pricing and Reimbursement

Sales of our products will depend, in part, on the extent to which the costs of our products will be covered by third-party payors, such as government healthcare programs, commercial insurance plans and managed healthcare organizations. These third-party payors are increasingly challenging the prices charged for medical products and services. Additionally, the containment of healthcare costs has become a priority for federal and state governments and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results.

Third-party payers continue to scrutinize and manage the prices charged for pharmaceutical products and services, and many also limit reimbursement for newly-approved or innovating products and indications. If these third-party payors do not consider our products to be cost-effective compared to other therapies, they may not cover our approved products as part of their plans' benefits or, if they do, they could apply utilization management restrictions, high patient cost-sharing obligations, or restrict the level of reimbursement, which may affect whether we can sell our products on a profitable basis.

Medicare is a U.S. federal healthcare program that provides coverage for certain healthcare items and services to individuals aged 65 years or older, as well as individuals of any age with certain disabilities and illnesses. Medicare Part D may affect reimbursement of our products upon approval. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which provide coverage for outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as part of Medicare Advantage plans. Part D prescription drug plan sponsors are not required to pay for all outpatient drugs, and each Part D plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D plan drug formularies must include at least two drugs within each therapeutic category and class of Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutics committee. Part D plan coverage and reimbursement may increase demand for our products for which we receive marketing approval. Moreover, while Part D provides prescription drug benefits only to Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in reimbursement by Medicare may result in a similar reduction in payments from non-governmental payors.

Medicaid is a U.S. healthcare program that provides coverage for certain healthcare items and services to low-income children, families, pregnant women and people with disabilities. It is jointly funded by the federal and state governments, and it is administered by individual states within parameters established by the federal government. Therefore, coverage and reimbursement for drugs may vary by state Medicaid program. A manufacturer must enter into a Medicaid Drug Rebate Agreement to have its products covered by Medicaid. Under the Medicaid program, and per the Medicaid Drug Rebate Agreement, manufacturers agree to report certain prices to the government and pay rebates to state Medicaid programs based on Medicaid utilization of the manufacturer's covered drugs.

In addition to the Medicaid Drug Rebate Program, federal law requires companies to participate in the Public Health Service's 340B Drug Pricing Program in order to have the manufacturer's drugs covered under Medicaid. The 340B Drug Pricing Program requires participating manufacturers to charge statutorily-defined covered entities no more than the 340B ''ceiling price'' for the manufacturer's covered outpatient drugs. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010 (collectively, the ''ACA''), extended eligibility to participate in the 340B program to certain additional types of hospitals (including critical access hospitals, sole community hospitals, rural referral centers and freestanding cancer hospitals). For purposes of these newly eligible covered entities, the ACA specifically excluded from the definition of ''covered outpatient drugs'' certain drugs designated as ''orphan drugs'' under section 526 of the FDCA. We are also required to discount such products to authorized users of the Federal Supply Schedule of the General Services Administration, under which additional laws and requirements apply. These programs require submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, and the guidance governing such calculations is not always clear. Compliance with such requirements can require significant investment in personnel, systems and resources, but failure to properly calculate prices, or offer required discounts or rebates can subject manufacturers to substantial penalties.

In March 2010, the ACA became law in the United States. Among other things, the ACA was enacted to expand access and increase consumer insurance protections while reducing the cost of health care for consumers, substantially changing the way health care is financed by both governmental and private insurers. The ACA also requires manufacturers to provide discounts on the prices of brand named drugs in the coverage gap under the Medicare Part D and increased the rebates paid by pharmaceutical companies on drugs covered by Medicaid. The ACA also imposes an annual fee, which increases annually, on sales by branded pharmaceutical manufacturers. Since its enactment, there have been a number of judicial, executive and

legislative challenges to the ACA, including recent tax legislation that removed the financial penalties for people who do not carry health insurance (known as the ‘‘individual mandate’’) and an Executive Order signed in October 2017 by President Trump directing federal agencies to modify how the ACA is implemented and announced that his administration will withhold the cost-sharing subsidies paid to health insurance exchange plans serving low-income enrollees. Congress may continue to consider legislation to repeal and replace some or all elements of the ACA. Additionally, a federal court in Texas ruled in December 2018 that the entire ACA is unconstitutional. Although that ruling is currently stayed and is being appealed, we cannot predict the outcome of this litigation, including a possible decision by the United States Supreme Court, and there is still uncertainty whether the ACA will undergo additional revisions. We cannot predict the impact of any future modifications.

There has been particular and increasing legislative and enforcement interest in the United States with respect to drug pricing practices, particularly with respect to drugs that have been subject to relatively large price increases over relatively short time periods. At the federal level, there have been several U.S. Congressional inquiries, proposed bills, and proposed administrative rules designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. The outcome and potential effects of these proposals is unclear, but Congress and the Trump administration have each indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing.

In addition, in some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before its cost may be funded within the respective national healthcare systems. The requirements governing drug pricing vary widely from country to country. For example, EU member states can restrict the range of medicinal products for which their national health insurance systems provide reimbursement and may control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profits the medicinal product generates for the company placing it on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products on cost-effectiveness grounds. Historically, products launched in countries in the European Union do not follow price structures of the United States and generally their prices tend to be significantly lower.

U.S. Fraud and Abuse Laws

Any present or future arrangements with third-party payors, healthcare providers and professionals and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may restrict certain marketing and contracting practices. These laws include, and are not limited to, anti-kickback and false claims statutes. Other pharmaceutical companies have settled alleged or admitted violations of these fraud and abuse laws with state and federal authorities in recent years and in some cases these settlements have amounted to hundreds of millions of dollars in damages, fines, and penalties, as well as the imposition of compliance program obligations through Corporate Integrity Agreements and other means. Lawsuits, or enforcement actions brought under fraud and abuse laws, can be extremely costly to defend, even if a company has strong defenses and ultimately succeeds in getting the allegations or enforcement action dismissed.

The federal Anti-Kickback Statute (42 U.S.C. §1320a-7b(b)) prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or providing remuneration, directly or indirectly, to induce either the referral of an individual, or the furnishing, recommending, or arranging for any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid. Remuneration is not defined in the federal Anti-Kickback Statute and has been broadly interpreted by regulators to include for example, cash payments, gifts, discounts, coupons, and the furnishing of free or discounted services or supplies. This statute has been broadly interpreted to apply to manufacturer arrangements with prescribers, purchasers, formulary managers and patients, among others.

The federal False Claims Act imposes civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. The government and *qui tam* relators have brought False Claims Act actions against pharmaceutical companies on the theory that their practices have caused false claims to be presented to the government. There is also a separate false claims provision imposing criminal penalties.

Other federal healthcare fraud-related laws also provide criminal liability for violations. The Criminal Healthcare Fraud statute (18 U.S.C. §1347) prohibits knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payers. Federal criminal law at 18 U.S.C. §1001, among other sections, prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

A number of states also have statutes or regulations similar to the federal Anti-Kickback Statute and False Claims Act that apply to items and services reimbursed under Medicaid and other state programs. Some state anti-kickback statutes apply not just to government payors, but to all payors, including commercial payors.

Other Laws

The Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act (collectively, ''HIPAA''), imposes obligations, on ''covered entities,'' including health plans and healthcare providers, and their business associates with respect to safeguarding the privacy, security and transmission of individually identifiable health information. Although drug manufacturers are not directly subject to HIPAA, we could be subject to criminal penalties if we knowingly obtain individually identifiable health information from a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. We are also subject to state, federal and international privacy and security laws governing the processing and security of personal identifiable information.

The federal Physician Payments Sunshine Act requirements under the ACA, and its implementing regulations, require manufacturers of drugs, devices, biologics and medical supplies to report to the U.S. Department of Health and Human Services information related to certain direct and indirect payments and other transfers of value made to covered recipients, such as physicians and teaching hospitals. Payments made to physicians and research institutions for clinical trials are included within the ambit of this law. We are also subject to similar laws in several states and various EU countries where we have operations. Additionally, several states have laws that prohibit manufacturers from providing certain payments or items of value to health care providers or other enumerated individuals or entities.

Employees

As of December 31, 2018, we had 483 employees, of which 330 were based in the United States and 153 were based outside the United States. None of our employees are represented by a labor union and we consider our employee relations to be good.

Corporate and Available Information

We were incorporated in Delaware in September 2002. Our principal executive offices are located at 10 Hudson Yards, 37th Floor, New York, NY 10001 and our telephone number is (646) 747-1000. We have several additional offices, including those in San Diego, California and London, United Kingdom. Our corporate website address is *www.interceptpharma.com.* We make available on our website, free of charge, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended (the ''Exchange Act''), as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission (''SEC''). Our SEC reports can be accessed through the Investors & Media section of our internet website. The references to *www.interceptpharma.com* herein are inactive textual references only, and the information found on our

internet website is not incorporated by reference into this Annual Report on Form 10-K or any other report we file with or furnish to the SEC. The SEC maintains an internet website that contains reports, proxy and information statements and other information about issuers, like us, that file electronically with the SEC. The address of that site is *http://www.sec.gov*.

Item 1A. Risk Factors

Investing in our securities involves a high degree of risk. The following risk factors and other information included in this Annual Report on Form 10-K should be carefully considered before deciding whether to invest in our securities. The risks and uncertainties described below and in our other filings are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. If any of the following risks, or such unknown risks, occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In that case, the market price of our securities could decline, and you may lose all or part of your investment.

Risks Related to Our Financial Position and Need for Additional Capital

We are currently dependent on the successful commercialization of Ocaliva for PBC. To the extent Ocaliva is not commercially successful, our business, financial condition and results of operations may be materially adversely affected and the price of our common stock may decline.

Ocaliva is our only drug that has been approved for sale and it has only been approved for the treatment of PBC in combination with UDCA in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA.

Our ability to generate profits from operations and become profitable currently depends on the commercial success of Ocaliva for PBC. However, the successful commercialization of Ocaliva for PBC is subject to many risks. We have not launched or commercialized a drug before, and there is no guarantee that we will be able to do so successfully. There are numerous examples of unsuccessful product launches and commercial efforts, as well as failures to meet expectations of market potential, including by pharmaceutical companies with greater experience and resources than us.

The commercial success of Ocaliva for PBC depends on the extent to which patients, physicians and payers accept and adopt Ocaliva as a treatment for PBC, and we do not know whether our or others' estimates in this regard will be accurate. As such, there is significant uncertainty in the degree of market acceptance that Ocaliva will have for PBC. For example, if the patient population suffering from PBC is smaller than we estimate, or even if the patient population matches our estimates but Ocaliva is not widely accepted as a treatment for PBC, the commercial potential of Ocaliva for PBC will be limited. Physicians may not prescribe Ocaliva and patients may be unwilling to use Ocaliva if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost. Additionally, the use of Ocaliva in a non-trial setting may result in the occurrence of unexpected or a greater incidence of side effects, adverse reactions or misuse that may negatively affect the commercial prospects of Ocaliva for PBC. Furthermore, any negative development in any other development program for OCA or our failure to satisfy the post-marketing regulatory commitments and requirements to which we are or may become subject, including the completion of our Phase 4 COBALT trial, may materially and adversely impact the commercial results and potential of Ocaliva for PBC. See ''— Risks Related to the Commercialization of Our Products'' and ''— Risks Related to the Development and the Regulatory Review and Approval of Our Products and Product Candidates'' below.

As a result, it is uncertain whether Ocaliva net sales for PBC will sustain our operations and it may take a significant amount of time before Ocaliva net sales for PBC sustain our operations. Furthermore, Ocaliva may not receive regulatory approval for PBC in jurisdictions beyond those in which it is currently approved, which may also limit our prospects. If the commercialization of Ocaliva for PBC is unsuccessful or perceived to be unsuccessful, the long-term prospects of Ocaliva for PBC, as well as the long-term prospects of our company, may be materially and adversely affected.

We have never been profitable. We expect to incur losses for the foreseeable future, and we may never achieve or sustain profitability.

We have never been profitable and do not expect to be profitable in the foreseeable future. We incurred net losses of $309.2 million, $360.4 million and $412.8 million for the years ended December 31, 2018, 2017 and 2016, respectively. To date, we have financed our operations primarily through public and private securities offerings, sales of product and payments received under our licensing and collaboration agreements. At December 31, 2018, we had $436.2 million in cash, cash equivalents and investment debt securities.

We have devoted substantially all of our resources to the development of our product candidates, including the conduct of our clinical trials, the launch and commercialization of Ocaliva for PBC, preparation for the potential launch of OCA for NASH and general and administrative operations, including the protection of our intellectual property.

We expect to continue to incur losses for the foreseeable future, and we expect these losses to be significant as we, among other things, continue to commercialize Ocaliva for PBC, develop and seek and maintain regulatory approvals for OCA for NASH and other indications, and build-out the infrastructure in the United States and internationally necessary to support our product development and commercialization efforts. We believe our prospects and ability to significantly grow revenues will be dependent on our ability to successfully develop and commercialize OCA for indications other than PBC, such as NASH. As a result, we expect a significant amount of resources to continue to be devoted to our development programs for OCA.

As part of our product development activities, we anticipate that we will continue our Phase 4 COBALT trial of Ocaliva for PBC. We also expect to continue our Phase 3 clinical program of OCA for NASH, including our Phase 3 REGENERATE trial in patients with liver fibrosis due to NASH through clinical outcomes in order to confirm clinical benefit and our Phase 3 REVERSE trial for NASH patients with compensated cirrhosis. We intend to evaluate the efficacy, safety and tolerability of bezafibrate in combination with OCA in patients with PBC in a Phase 2 study and to continue to develop OCA and our other existing product candidates, alone or in combination, for non-viral liver diseases in indications beyond NASH and PBC. Our overall development program for OCA for NASH is expected to include a number of trials, including clinical trials required to file for approval of OCA for NASH and to confirm clinical benefit. Our expenses could increase if we are required by the FDA or the EMA to perform studies or trials in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates.

If OCA or any of our other product candidates fails in clinical trials or does not gain or maintain regulatory approval, or if OCA or any of our other product candidates does not achieve market acceptance, we may never become profitable. Our net losses and negative cash flows 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 pharmaceutical product development and commercialization, we are unable to predict with certainty the timing or amount of our expenses, whether such expenses may increase, or when, or if, we will be able to achieve profitability. The amount of our future net losses will depend, in part, on our future expenses, whether and by how much such expenses increase and our ability to generate revenues.

We will require substantial additional funding, which may not be available to us on acceptable terms, if at all. If adequate funds are not available to us, we may be required to delay, limit, reduce or cease our operations.

We are currently advancing OCA through clinical development for multiple indications, including NASH, and other product candidates through various stages of clinical and preclinical development. Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. If, for example, the FDA, EMA or other regulatory authorities require that we perform additional studies beyond those that we currently expect, our expenses could increase materially beyond what we currently anticipate, and the timing of any potential product approval may be delayed.

In addition, we have incurred and anticipate that we will continue to incur significant research and development, product sales, marketing, manufacturing and distribution expenses relating to the commercialization of Ocaliva for PBC and OCA for NASH, if approved. As part of our longer-term strategy, we anticipate that we will incur significant expenses in connection with our research and development efforts, the commercialization of our approved products other than Ocaliva for PBC and OCA for NASH, if approved, and the build-out of our general and administrative infrastructure in the United States and abroad. We may also engage in business development activities that involve potential in- or out-licensing of products or technologies or acquisitions of other products, technologies or businesses.

As of December 31, 2018, we had $436.2 million in cash, cash equivalents and investment debt securities. We currently expect to continue to incur significant operating expenses in the fiscal year ending December 31, 2019. These expenses are planned to support, among other initiatives, the continued

commercialization of Ocaliva for PBC in the United States and our other markets, our continued clinical development of OCA for PBC and NASH and our other earlier stage research programs. Although we believe that our existing capital resources, together with our net sales of Ocaliva for PBC, will be sufficient to fund our anticipated operating requirements for the next twelve months, we may need to raise additional capital to fund our operating requirements beyond that period. Furthermore, in light of the numerous risks and uncertainties associated with pharmaceutical product development and commercialization, any delays in, or unanticipated costs associated with, our development, regulatory or commercialization efforts could significantly increase the amount of capital required by us to fund our operating requirements. Accordingly, we may seek to access the public or private capital markets whenever conditions are favorable, even if we do not have an immediate need for additional capital at that time. Our forecast regarding the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results, including the costs to maintain our currently planned operations, could vary materially.

Our forecasts regarding the period of time that our existing capital resources will be sufficient to meet our operating requirements and the timing of our future funding requirements, both near and long-term, will depend on a variety of factors, many of which are outside of our control. Such factors include, but are not limited to:

- our ability to successfully commercialize Ocaliva for PBC;
- our ability to maintain our regulatory approval of Ocaliva for PBC in the United States, Europe, Canada, Israel, Australia and other jurisdictions in which we have or may receive marketing authorization;
- the initiation, timing, cost, conduct, progress and results of our research and development activities, preclinical studies and clinical trials, including any issues, delays or failures in identifying patients, enrolling patients, treating patients, meeting specific endpoints in the jurisdictions in which we intend to seek approval or completing and timely reporting the results of our NASH or PBC clinical trials;
- our ability to timely and cost-effectively file for and obtain regulatory approval of our product candidates, including OCA for NASH, in the United States, Europe and our other target markets;
- conditions that may be imposed by regulatory authorities on our marketing approvals for our products and product candidates, such as the need for clinical outcomes data (and not just results based on achievement of a surrogate endpoint), and any related restrictions, limitations and/or warnings contained in the label of any of our products or product candidates;
- any potential side effects associated with Ocaliva for PBC, OCA for NASH or our other product candidates that could delay or prevent approval, require that an approved product be taken off the market, require the inclusion of safety warnings or precautions or otherwise limit the sale of such product or product candidate;
- our ability to establish and maintain relationships with, and the performance of, third-party manufacturers, contract research organizations and other vendors upon whom we are substantially dependent for, among other things, the manufacture and supply of our products, including Ocaliva for PBC and, if approved, OCA for NASH, and our clinical trial activities;
- our ability to identify, develop and successfully commercialize our products and product candidates, including our ability to timely and successfully launch OCA for NASH, if approved;
- our ability to obtain and maintain intellectual property protection for our products and product candidates, including our ability to cost-effectively file, prosecute, defend and enforce any patent claims or other intellectual property rights;
- the size and growth of the markets for our products and product candidates and our ability to serve those markets;

- the degree of market acceptance of Ocaliva for PBC and, if approved, OCA for NASH or our other product candidates among physicians, patients and healthcare payors;
- the availability of adequate coverage and reimbursement from governmental and private healthcare payors for our products, including Ocaliva for PBC and, if approved, OCA for NASH, and our ability to obtain adequate pricing for such products;
- our ability to establish and maintain effective sales, marketing and distribution capabilities, either directly or through collaborations with third parties;
- competition from existing drugs or new drugs that become available;
- our ability to prevent system failures, data breaches or violations of data protection laws;
- costs and outcomes relating to any disputes, governmental inquiries or investigations, legal proceedings or litigation, including any securities, intellectual property, employment, product liability or other litigation;
- our collaborators' election to pursue research, development and commercialization activities;
- our ability to establish and maintain relationships with collaborators with development, regulatory and commercialization expertise;
- our need for and ability to generate or obtain additional financing;
- our estimates regarding future expenses, revenues and capital requirements and the accuracy thereof;
- our use of cash and short-term investments;
- our ability to acquire, license and invest in businesses, technologies, product candidates and products;
- our ability to attract and retain key personnel to manage our business effectively;
- our ability to manage the growth of our operations, infrastructure, personnel, systems and controls;
- our ability to obtain and maintain adequate insurance coverage;
- the impact of general U.S. and foreign economic, industry, market, regulatory or political conditions, including the potential impact of Brexit; and
- the other risks and uncertainties identified under the captions ''Risk Factors,'' ''Business'' and ''Management's Discussion and Analysis of Financial Condition and Results of Operations'' and elsewhere in this Annual Report on Form 10-K and in our other periodic filings filed with the SEC.

We have no committed external sources of funding and additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available to us, we may not be able to make scheduled debt payments on a timely basis, or at all, and may be required to delay, limit, reduce or cease our operations.

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

Unless and until we generate sufficient cash flow from sales of our products, including Ocaliva for PBC and, if approved, OCA for NASH, we expect to finance our future cash needs through public or private equity offerings, debt financings, government or other third-party funding, marketing and distribution arrangements or other collaborations, strategic alliances and licensing arrangements, or a combination of these sources. Additional funding may not be available to us on acceptable terms, if at all.

The terms of any future financing may adversely affect the interests of our existing securityholders. For example, to the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such

as incurring additional debt, making capital expenditures or declaring dividends. We also could be required to seek funds through arrangements with licensing or collaborative partners or otherwise that may require us to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We have a limited operating history as a commercial organization, which may make it difficult to predict our future performance, and we expect to continue to face a number of factors that may cause operating results to fluctuate.

We are a biopharmaceutical company with a limited operating history as a commercial organization. Prior to the launch and commercialization of Ocaliva for PBC, our operations were limited to developing our technology, undertaking preclinical studies and clinical trials of our product candidates and preparing for the commercial launch of Ocaliva for PBC. Other than Ocaliva for PBC, none of our other product candidates have received regulatory approval. Consequently, any predictions regarding our future success or viability may not be as accurate as they could be if we had a longer operating history or greater experience commercializing approved products.

The commercialization of Ocaliva for PBC has been and will continue to be, and, if approved, the commercialization of OCA for NASH will be, expensive and time-consuming, and we cannot be certain that we will be able to generate sufficient revenues from sales of Ocaliva for PBC and, if approved, OCA for NASH in our target markets to offset such costs. Furthermore, our financial condition and operating results have varied significantly in the past and are expected to continue to significantly fluctuate from quarter-to-quarter and year-to-year due to a variety of factors, many of which are outside of our control. Such factors include, but are not limited to:

- our ability to successfully commercialize Ocaliva for PBC;
- our ability to maintain our regulatory approval of Ocaliva for PBC in the United States, Europe, Canada, Israel, Australia and other jurisdictions in which we have or may receive marketing authorization;
- the initiation, timing, cost, conduct, progress and results of our research and development activities, preclinical studies and clinical trials, including any issues, delays or failures in identifying patients, enrolling patients, treating patients, meeting specific endpoints in the jurisdictions in which we intend to seek approval or completing and timely reporting the results of our NASH or PBC clinical trials;
- our ability to timely and cost-effectively file for and obtain regulatory approval of our product candidates, including OCA for NASH, in the United States, Europe and our other target markets;
- conditions that may be imposed by regulatory authorities on our marketing approvals for our products and product candidates, such as the need for clinical outcomes data (and not just results based on achievement of a surrogate endpoint), and any related restrictions, limitations and/or warnings contained in the label of any of our products or product candidates;
- any potential side effects associated with Ocaliva for PBC, OCA for NASH or our other product candidates that could delay or prevent approval, require that an approved product be taken off the market, require the inclusion of safety warnings or precautions or otherwise limit the sale of such product or product candidate;
- our ability to establish and maintain relationships with, and the performance of, third-party manufacturers, contract research organizations and other vendors upon whom we are substantially dependent for, among other things, the manufacture and supply of our products, including Ocaliva for PBC and, if approved, OCA for NASH, and our clinical trial activities;
- our ability to identify, develop and successfully commercialize our products and product candidates, including our ability to timely and successfully launch OCA for NASH, if approved;

- our ability to obtain and maintain intellectual property protection for our products and product candidates, including our ability to cost-effectively file, prosecute, defend and enforce any patent claims or other intellectual property rights;
- the size and growth of the markets for our products and product candidates and our ability to serve those markets;
- the degree of market acceptance of Ocaliva for PBC and, if approved, OCA for NASH or our other product candidates among physicians, patients and healthcare payors;
- the availability of adequate coverage and reimbursement from governmental and private healthcare payors for our products, including Ocaliva for PBC and, if approved, OCA for NASH, and our ability to obtain adequate pricing for such products;
- our ability to establish and maintain effective sales, marketing and distribution capabilities, either directly or through collaborations with third parties;
- competition from existing drugs or new drugs that become available;
- our ability to prevent system failures, data breaches or violations of data protection laws;
- costs and outcomes relating to any disputes, governmental inquiries or investigations, legal proceedings or litigation, including any securities, intellectual property, employment, product liability or other litigation;
- our collaborators' election to pursue research, development and commercialization activities;
- our ability to establish and maintain relationships with collaborators with development, regulatory and commercialization expertise;
- our need for and ability to generate or obtain additional financing;
- our estimates regarding future expenses, revenues and capital requirements and the accuracy thereof;
- our use of cash and short-term investments;
- our ability to acquire, license and invest in businesses, technologies, product candidates and products;
- our ability to attract and retain key personnel to manage our business effectively;
- our ability to manage the growth of our operations, infrastructure, personnel, systems and controls;
- our ability to obtain and maintain adequate insurance coverage;
- the impact of general U.S. and foreign economic, industry, market, regulatory or political conditions, including the potential impact of Brexit; and
- the other risks and uncertainties identified under the captions ''Risk Factors,'' ''Business'' and ''Management's Discussion and Analysis of Financial Condition and Results of Operations'' and elsewhere in this Annual Report on Form 10-K and in our other periodic filings filed with the SEC.

Risks Related to the Development and the Regulatory Review and Approval of Our Products and Product Candidates

We cannot be certain whether Ocaliva will receive full approval for PBC in jurisdictions where it has previously received accelerated or conditional approval, or that Ocaliva will be approved for PBC in any jurisdictions beyond those in which it is currently approved. Furthermore, OCA may not be approved for NASH or any other indication beyond PBC and we may not receive regulatory approval for any other product candidate. Without regulatory approval, we will not be able to market and commercialize our product candidates.

The development, testing, manufacture, labeling, packaging, storage, approval, promotion, advertising, distribution, marketing and export and import, among other things, of our products and product candidates are subject to extensive regulation by the FDA in the United States, the EMA in Europe and various regulatory

authorities in other countries, with regulations differing from country to country. We are not permitted to market our product candidates in the United States or Europe until we receive approval of an NDA, from the FDA, or an MAA, from the EMA, respectively. Currently, our ability to generate product sales depends on the successful marketing of Ocaliva for PBC in the jurisdictions in which it has received regulatory approval. In the future, our ability to generate product sales in addition to those of Ocaliva for PBC will depend on whether we are successful in obtaining regulatory approval of our other product candidates, including OCA for NASH.

Ocaliva is our only drug that has been approved for sale and it has only been approved for the treatment of PBC in combination with UDCA in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA. In the United States, Ocaliva was approved for PBC under the accelerated approval pathway. Accelerated approval was granted for Ocaliva for PBC based on a reduction in ALP; however, an improvement in survival or disease-related symptoms has not yet been established. Continued approval of Ocaliva for PBC in the United States may be contingent upon the verification and description of clinical benefit in confirmatory trials. Our Phase 4 COBALT confirmatory outcomes trial may fail to show a clinical benefit for Ocaliva for PBC or may not satisfy applicable regulatory requirements for other reasons. As specified by the applicable post-marketing requirements, our COBALT trial includes subjects across the spectrum of PBC disease, including early and advanced PBC. We have agreed to evaluate the safety and efficacy of Ocaliva in patients with moderate to severe hepatic impairment and as a monotherapy in patients with PBC. In addition, we have agreed to develop and characterize a lower dose formulation of Ocaliva to allow for once daily dosing in patients with moderate or advanced hepatic impairment.

We commenced our commercial launch of Ocaliva for PBC in certain European countries in 2017 following the European Commission's grant of conditional approval in December 2016. Our marketing authorization in the European Union is conditioned on the completion of the COBALT trial and a trial evaluating the safety and efficacy of Ocaliva in patients with moderate to severe hepatic impairment.

Since January 2017, Ocaliva has also received regulatory approval in several of our target markets outside the United States and Europe, including Canada, Israel and Australia, and we are pursuing marketing approval of Ocaliva for PBC in our other international target markets. If obtained, continued approval of Ocaliva for PBC in such jurisdictions may be contingent upon the verification and description of clinical benefit in confirmatory trials. Any delay or failure in satisfying the post-marketing regulatory commitments and requirements to which we are or may become subject, including our Phase 4 COBALT trial, may jeopardize the continued approval of Ocaliva for PBC in the United States, European Union and other jurisdictions.

Ocaliva is not approved for any indication other than PBC. We currently have no other products approved for sale and we cannot guarantee that we will ever have additional marketable products or that OCA will be approved for use in additional indications such as NASH. NDAs and MAAs must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety and effectiveness for each desired indication. NDAs and MAAs must also include significant information regarding the chemistry, manufacturing and controls for the product. Obtaining approval of an NDA or an MAA is a lengthy, expensive and uncertain process, and we may not be successful in obtaining approval. The FDA and the EMA review processes can take years to complete and approval is not guaranteed. Even after the submission of an NDA, the FDA must decide whether to accept the submission for filing and review. In addition, in June 2016, eligible members of the electorate in the United Kingdom decided by referendum to leave the European Union, in what is often referred to as ''Brexit''. Because a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, Brexit could materially change the regulatory regime applicable to our operations, including with respect to Ocaliva for PBC and, if approved, OCA for NASH and our other product candidates.

As is the case with the approval of Ocaliva for PBC, approvals may be conditional upon the completion of one or more clinical trials. In addition, delays in approvals or rejections of marketing applications in the United States, Europe or other countries may be based upon many factors, including, for example, regulatory requests for additional analyses, reports, data, preclinical studies and clinical trials, regulatory questions regarding safety, different interpretations of data and results, changes in regulatory policy during the period of

product development and the emergence of new information regarding our product candidates or approved products. Initial and continued regulatory approval is also dependent on successfully passing regulatory inspection requirements applicable to us, our clinical sites and our key vendors, including requirements that we and such parties comply with applicable good clinical, pharmacovigilance, laboratory and manufacturing practices regulations. Critical findings could jeopardize or delay the approval of our NDAs or MAAs or impair our ability to maintain our marketing approvals.

Prior to receiving regulatory approval, we must finalize the product label for each of our product candidates in each jurisdiction in which we seek regulatory approval. Even if our product is approved, the FDA, EMA or other applicable regulatory authority may limit the indications or uses for which our product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming clinical trials, risk mitigation programs or reporting as a condition of approval. Also, regulatory approval for our approved products may be withdrawn. Obtaining regulatory approval for the marketing of our product in one country does not ensure that we will be able to obtain regulatory approval for such product in any other country.

In order to obtain regulatory approval for OCA for indications other than PBC, we will need to complete a number of additional clinical trials and studies. For example, in connection with our Phase 3 clinical program of OCA for NASH, we are currently conducting our Phase 3 REGENERATE trial in patients with liver fibrosis due to NASH through clinical outcomes in order to confirm clinical benefit and our Phase 3 REVERSE trial for NASH patients with compensated cirrhosis. Our ability to obtain and maintain the regulatory approvals necessary to commercialize OCA for indications other than PBC, including NASH, will depend on our ability to successfully design, conduct and complete these trials, the efficacy and safety profile of OCA demonstrated by such trials and our ability to prepare and submit complex regulatory filings in accordance with applicable regulatory requirements.

There can be no assurance that OCA will receive marketing approval for PBC in jurisdictions where it has not yet been approved or for NASH in any jurisdiction, or that any of our other product candidates will receive marketing approval for any indication in any jurisdiction. We cannot predict whether our clinical trials and studies for our product candidates, including OCA for PBC, NASH or any other indication, will be successful, whether regulatory authorities will agree with our conclusions relating to the clinical trials and studies we conduct, or whether such regulatory authorities will require us to conduct additional clinical trials or studies. For example, while OCA received breakthrough therapy designation from the FDA in January 2015 for the treatment of NASH patients with liver fibrosis and we currently intend to file for approval of OCA for NASH in the United States based on the results from the 18-month analysis of our Phase 3 REGENERATE trial in patients with liver fibrosis due to NASH, we do not know if one pivotal clinical trial will be sufficient for marketing approval in the United States or if the FDA will approve OCA for NASH patients with liver fibrosis on an accelerated basis, or at all. Our Phase 3 REGENERATE trial remains blinded after the interim analysis and will continue to follow patients until the occurrence of a pre-specified number of adverse liver-related clinical events, including progression to cirrhosis, to confirm clinical benefit on a post-marketing basis, if approved.

Furthermore, the Phase 2 dose ranging trial of OCA in 200 adult NASH patients in Japan conducted by our collaborator, Sumitomo Dainippon, did not meet statistical significance for the primary endpoint. The primary endpoint in the Sumitomo Dainippon trial was histologic improvement defined as at least a two-point improvement in NAS with no worsening of fibrosis. In this trial, there was a dose dependent, although not statistically significant, increase in the percentage of OCA-treated patients compared to placebo who achieved the primary endpoint ($p = 0.053$). In addition, no difference was seen in fibrosis improvement in the OCA groups compared to placebo. Sumitomo Dainippon may not initiate any registrational trials in NASH and the results of any additional trial conducted by Sumitomo Dainippon may not result in an improvement when compared to the results of its Japanese Phase 2 dose ranging trial.

If we are unable to obtain regulatory approval for OCA for PBC in the jurisdictions in which it is not currently approved or obtain regulatory approval in the United States, European Union and other jurisdictions for OCA for other indications, such as NASH, or for our other product candidates, we may not be able to generate sufficient revenue to become profitable or to continue our operations.

We are developing product candidates for the treatment of rare diseases or diseases for which there are no or limited therapies, such as PBC and NASH, and for some of which there is little clinical experience, and our development approach involves new endpoints and methodologies. As a result, there is a heightened risk that we will not be able to gain agreement with regulatory authorities regarding an acceptable development plan, that the outcome of our clinical trials will not be favorable or that, even if favorable, regulatory authorities may not find the results of our clinical trials to be sufficient for marketing approval.

We are focused on developing therapeutics for the treatment of rare diseases and diseases for which there are no or limited treatments. As a result, the design and conduct of our clinical trials for these indications is subject to heightened risk.

In the United States, the FDA generally requires two adequate and well-controlled pivotal clinical trials to approve an NDA. Furthermore, for full approval of an NDA, the FDA requires a demonstration of efficacy based on a clinical benefit endpoint. The FDA may grant accelerated approval based on a surrogate endpoint reasonably likely to predict clinical benefit. Even though our pivotal clinical trials for a specific indication, such as our Phase 3 REGENERATE trial of OCA in patients with liver fibrosis due to NASH, may achieve their primary endpoints and are reasonably believed by us to be likely to predict clinical benefit, the FDA may not accept the results of such trials or approve our product candidate on an accelerated basis, or at all. It is also possible that the FDA may refuse to accept for filing and review any regulatory application we submit for regulatory approval in the United States, including any regulatory application we submit for NASH. Even if our regulatory application is accepted for review, there may be delays in the FDA's review process and the FDA may determine that such regulatory application does not support the approval of the product candidate. In such a case, the FDA may issue a complete response letter that may require that we conduct and/or complete additional clinical trials and preclinical studies or provide other additional information or data before it will reconsider our application for approval. Any such requirements may be substantial, expensive and time-consuming, and there is no guarantee that the FDA will ultimately decide that any such regulatory application supports the approval of the product candidate. The FDA may also refer any regulatory application, such as any regulatory application we may file for OCA for NASH, to an advisory committee for review and recommendation as to whether, and under what conditions, the application should be approved. While the FDA is not bound by the recommendation of an advisory committee, it considers such recommendations carefully when making decisions.

Even if we receive accelerated approval for any of our product candidates, we may be required to conduct or complete a post-approval clinical outcomes trial to confirm the clinical benefit of such product candidates by demonstrating the correlation of the surrogate endpoint therapeutic response in patients with a significant reduction in adverse clinical outcomes over time. For example, as a condition of the accelerated approval of Ocaliva for PBC in the United States, we are required to conduct a clinical outcomes study with respect to Ocaliva for PBC. Following discussions with regulatory authorities, we initiated our COBALT clinical outcomes confirmatory trial for PBC in December 2014 prior to the approval of Ocaliva for PBC. The COBALT trial includes subjects across the spectrum of PBC disease, including early and advanced PBC. We have agreed to evaluate the safety and efficacy of Ocaliva in patients with moderate to severe hepatic impairment and as a monotherapy in patients with PBC. There can be no assurance that our COBALT trial conducted as part of our post-marketing obligations will confirm that the surrogate endpoint used for accelerated approval of Ocaliva for PBC will eventually show an adequate correlation with clinical outcomes. If any such trial fails to show such adequate correlation, we may not be able to maintain our previously granted marketing approval of Ocaliva for PBC. Similarly, if approved based on a surrogate endpoint, continued approval of OCA for other indications, or of any of our other product candidates, may be contingent upon the verification and description of clinical benefit in confirmatory trials.

Our marketing authorization in the European Union for Ocaliva for the treatment of PBC is not a full approval. Instead, it is conditional on the conduct of certain post-approval studies. Our ability to maintain conditional marketing authorization of Ocaliva for PBC in the European Union is limited to specific circumstances and subject to several conditions and obligations that we may be unable to satisfy in whole or at all, including the completion of one or more clinical outcomes trials to confirm the clinical benefit of Ocaliva for PBC. Conditional marketing authorizations based on incomplete clinical data may be granted for a limited number of listed medicinal products for human use, including products designated as orphan medicinal

products under European Union law, if (i) the risk-benefit balance of the product is positive, (ii) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (iii) unmet medical needs will be fulfilled and (iv) the benefit to public health of the immediate availability on the market of the medicinal product outweighs the risk inherent in the fact that additional data are still required. Specific obligations, including obligations relating to the successful completion of ongoing or new studies and the collection of pharmacovigilance data, may be specified in the conditional marketing authorization. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions.

Our ongoing Phase 3 REGENERATE trial of OCA in patients with liver fibrosis due to NASH incorporates an interim primary surrogate endpoint that may serve as the basis for a regulatory submission for accelerated approval in the United States and conditional approval in Europe. Accelerated approval in the United States and conditional approval in the European Union for OCA for NASH are subject to similar risks as discussed above in relation to OCA for PBC. In the REGENERATE primary efficacy analysis, once-daily OCA 25 mg met, with statistical significance, the primary endpoint agreed with the FDA of fibrosis improvement by at least one stage with no worsening of NASH (defined as no worsening of hepatocellular ballooning, no worsening of lobular inflammation and no worsening of steatosis) at the planned 18-month analysis. Although a numerically greater proportion of patients in both OCA treatment arms compared to placebo achieved the primary endpoint of NASH resolution with no worsening of liver fibrosis in the primary efficacy analysis, this result did not reach statistical significance. As agreed with the FDA, in order for the primary objective to be met, the study was required to achieve one of the two primary endpoints. In November 2018, the EMA issued draft regulatory guidance in which it presented its preliminary views with respect to various NASH clinical development matters, including with respect to potential surrogate endpoints, and requested comments thereon by August 2019. Although we did not reach agreement with the EMA on the definition and analysis of a surrogate endpoint prior to the readout of the 18-month analysis of the REGENERATE trial, we believe that the totality of the REGENERATE data supports the submission of an MAA with the EMA. However, the data that we submit to the EMA may not ultimately be found by the EMA to be sufficient for marketing approval.

While OCA received breakthrough therapy designation from the FDA in January 2015 for the treatment of NASH patients with liver fibrosis and we currently intend to file for approval of OCA for NASH in the United States based on the results from the 18-month interim analysis of our Phase 3 REGENERATE trial in patients with liver fibrosis due to NASH, we do not know if one pivotal clinical trial will be sufficient for marketing approval in the United States or if the FDA will approve OCA for NASH patients with liver fibrosis on an accelerated basis, or at all. In addition, our regulatory submission may not be accepted by the FDA for review and, even if accepted for review, there may be delays in the FDA's review process or the FDA may determine that our submission does not support the approval of OCA for the treatment of NASH. Before granting approval, the FDA may also require that we continue our Phase 3 REGENERATE trial until completion to assess the potential benefits of OCA treatment on liver-related and other clinical outcomes. Our regulatory pathway for OCA for the treatment of NASH will depend upon our discussions with the FDA and EMA. As a result, we may face difficulty in establishing an acceptable registration strategy with respect to our Phase 3 REGENERATE trial, as well as other trials we may conduct in other subpopulations of NASH patients.

If we continue the development of OCA for PSC, we may seek marketing approval based on a surrogate endpoint. While the EMA issued draft regulatory guidance in November 2018, the FDA has not issued formal guidance regarding a validated surrogate endpoint as a basis for seeking approval in PSC. Identifying an acceptable surrogate endpoint may take longer than we expect and any surrogate endpoint we select may ultimately not be accepted by the FDA, EMA or other applicable regulatory authorities.

Prior to any approval of OCA for NASH or OCA for PBC in jurisdictions in which it is not currently approved or the approval of our other product candidates, the FDA, EMA or other applicable regulatory authorities may require additional preclinical studies and/or clinical trials, which may be expensive and time consuming to conduct and complete. Consequently, any such requirement that we conduct additional preclinical studies or clinical trials could materially and adversely affect our business, financial condition and results of operations. Furthermore, even if we receive such approval, the relevant labeling may include

restrictions, limitations and/or warnings that could impact the commercial success of OCA or our other product candidates in the applicable markets.

Delays or difficulties in the commencement, enrollment and completion of our clinical trials and studies could increase our product development costs and delay, limit or prevent us from obtaining regulatory approval for OCA and our other product candidates.

Delays or difficulties in the commencement, enrollment and completion of our clinical trials and studies could increase our product development costs and limit or prevent us from obtaining regulatory approval for OCA and our other product candidates. We are currently conducting a number of clinical trials, including our Phase 4 COBALT clinical outcomes confirmatory trial of Ocaliva for PBC, our Phase 3 REGENERATE trial of OCA in patients with liver fibrosis due to NASH through clinical outcomes in order to confirm clinical benefit and our Phase 3 REVERSE trial of OCA for NASH patients with compensated cirrhosis. We are also conducting our CARE trial of OCA in pediatric patients with biliary atresia as a part of an EMA-approved PIP supporting the conditional approval of Ocaliva for PBC. The results from these clinical trials and our other clinical trials and studies may not be available when we anticipate and we may be required to conduct additional clinical trials or studies not currently planned in order for our product candidates, including OCA for PBC and NASH, to be approved. In addition, our clinical programs are subject to a number of risks and uncertainties, such as the results of other trials, patient enrollment, safety issues or regulatory interactions that result in a change of trial design or timing. Consequently, we do not know whether our current or future clinical trials or studies of OCA or our other product candidates will begin or be completed on schedule, if at all.

The commencement, enrollment and completion of our clinical trials and studies may be delayed, suspended or otherwise adversely affected for a variety of reasons, including:

- our inability to obtain sufficient funds to complete or continue our clinical trials;
- our inability to reach agreements on acceptable terms with prospective contract research organizations (“CROs”) and trial sites, the terms of which may be subject to extensive negotiation and may vary significantly among our various CROs and trial sites;
- clinical holds, other regulatory objections to our commencing or continuing a clinical trial or our inability to obtain regulatory approval to commence clinical trials in countries that require such approvals;
- our discussions with the FDA, EMA or other regulatory authorities prior to, or following, the initiation of our clinical trials, regarding, among other matters, the scope or design of our clinical trials, including trial endpoints, protocols and statistical analysis plans, and any modifications thereto;
- our inability to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs, including some that may be for the same indications targeted by our product candidates;
- any delay in receiving results from, or failure to achieve the necessary results in, our clinical trials;
- our inability to obtain approval from institutional review boards or independent ethics committees to conduct our clinical trials at their respective sites;
- any data monitoring committee recommendation that our clinical trials be modified, suspended or terminated due to safety, lack of efficacy or other reasons;
- severe or unexpected drug-related adverse events experienced by patients or any determination that a clinical trial presents unacceptable health risks;
- any breach of the terms of any relevant agreement by us, our current or future collaborators that have responsibility for the clinical development of any of our product candidates, including Sumitomo Dainippon, or investigators conducting clinical trials on our product candidates;

- our inability to timely manufacture, or obtain from our contract manufacturers, sufficient quantities of our product candidate required for our clinical trials; and
- any difficulty recruiting, enrolling or retaining patients in our clinical trials based on, among other factors, the enrollment criteria for our clinical trials, the rarity of the disease, the characteristics of the population being studied, the risks of the procedures that may be required as part of the clinical trials, such as a liver biopsy, or competition from other clinical trial programs recruiting patients for the same indications as our product candidates.

For example, our Phase 3 REGENERATE trial is a large and complicated clinical trial in a disease without any approved therapies and involves serial liver biopsies over many years. While we announced topline results from the 18-month analysis of our pivotal Phase 3 REGENERATE trial in February 2019, REGENERATE is planned to continue through clinical outcomes in order to confirm clinical benefit and there can be no assurance that we will retain a sufficient number of patients in the full study cohort or complete the clinical outcomes trial in accordance with the study protocol or on a timely basis. As we engage in other large and complicated trials and trials in advanced disease populations, we may experience a number of challenges that may negatively affect or delay our plans and development programs.

Additionally, we have in the past occasionally experienced difficulties retaining patients enrolled in our clinical trials. Difficulties in enrolling and retaining patients may delay our clinical trials or result in negative or inconclusive outcomes, and we or our collaborators may decide, or regulatory authorities may require us, to conduct additional clinical trials or additional analyses of existing clinical trials. Any delay or compromises with respect to the validity of our clinical trials may have a material adverse effect on our business or decrease our competitive position relative to other biotechnology or pharmaceutical companies with whom we compete.

In addition, if we or any of our collaborators are required to conduct additional clinical trials or other preclinical studies of our product candidates beyond those contemplated, our ability to obtain regulatory approval of these product candidates and generate revenue from their sales would be similarly harmed.

Clinical failure can occur at any stage of clinical development. The results of earlier clinical trials are not necessarily predictive of future results and any product candidate we or our collaborators advance through clinical trials, including OCA, may not have favorable results in later clinical trials or receive regulatory approval.

Clinical failure can occur at any stage of clinical development. Clinical trials may produce negative or inconclusive results, and we or our collaborators may decide, or regulators may require us, to conduct additional clinical trials or preclinical studies. In addition, data obtained from trials and studies are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may delay, limit or prevent regulatory approval. Success in preclinical studies and early clinical trials does not ensure that subsequent clinical trials will generate the same or similar results or otherwise provide adequate data to demonstrate the efficacy and safety of our product candidates. A number of companies in the pharmaceutical industry, including those with greater resources and experience than us, have suffered significant setbacks in Phase 3 clinical trials and at other stages of clinical development, even after seeing promising results in earlier clinical trials.

In addition, the design of clinical trials, including trial endpoints, protocols and statistical analysis plans, can determine whether such trials will support product approvals, and flaws in the design of such trials may not become apparent until such trials are well-advanced. We may be unable to design and execute a clinical trial to support regulatory approval. Further, clinical trials of product candidates often reveal that it is not practical or feasible to continue development efforts. If OCA or our other product candidates are found to be unsafe or lack efficacy for any indication, we will not be able to obtain regulatory approval for them, and our prospects and business may be materially and adversely affected.

There may be significant variability in the safety and/or efficacy results we see in different trials studying OCA or our other product candidates due to numerous factors, including differences in the underlying disease being studied, changes or differences in trial protocols or statistical analysis plans, differences in the composition of the patient populations or clinical trial sites, differences in adherence to the dosing regimen

and other aspects of the trial protocols and differences in the rate of dropouts among clinical trial participants. We do not know whether any Phase 2, Phase 3 or other clinical trials we or any of our collaborators may conduct on our product candidates will demonstrate consistent or adequate efficacy and safety or result in the approval of our product candidates by regulatory authorities. If we are unable to bring any of our current or future product candidates to market, or to acquire any previously approved products, our ability to create long-term stockholder value will be limited.

Although Ocaliva for PBC has received accelerated approval in the United States and conditional approval in the European Union, its full approval depends on the completion and results of post-marketing clinical trials, including our Phase 4 COBALT trial. We cannot assure you that these trials will demonstrate a correlation of the surrogate endpoint therapeutic response in patients taking Ocaliva for PBC with a significant reduction in adverse clinical outcomes over time.

In December 2014, we received comprehensive datasets from the Phase 2b FLINT trial for the treatment of NASH, which met its primary endpoint with statistical significance. In October 2015, we announced that the Phase 2 dose ranging trial of OCA in 200 adult NASH patients in Japan conducted by our collaborator, Sumitomo Dainippon, did not meet its primary endpoint with statistical significance. In the Sumitomo Dainippon trial, there was a dose dependent, although not statistically significant, increase in the percentage of OCA-treated patients compared to placebo who achieved the primary endpoint ($p = 0.053$). In addition, no difference was seen in fibrosis improvement in the OCA groups compared to placebo. The Sumitomo Dainippon Phase 2 trial involved different doses of OCA being administered to the trial subjects than those utilized in the Phase 2b FLINT trial. Furthermore, the baseline characteristics between the patients in the Japanese Phase 2 dose ranging trial conducted by Sumitomo Dainippon were distinct in a number of ways from those of the Western patients included in the Phase 2b FLINT trial.

In February 2019, we announced topline results from the 18-month analysis of our pivotal Phase 3 REGENERATE trial in patients with liver fibrosis due to NASH. In the primary efficacy analysis, once-daily OCA 25 mg met, with statistical significance, the primary endpoint agreed with the FDA of fibrosis improvement by at least one stage with no worsening of NASH (defined as no worsening of hepatocellular ballooning, no worsening of lobular inflammation and no worsening of steatosis) at the planned 18-month analysis. Although a numerically greater proportion of patients in both OCA treatment arms compared to placebo achieved the primary endpoint of NASH resolution with no worsening of liver fibrosis in the primary efficacy analysis, this result did not reach statistical significance. As agreed with the FDA, in order for the primary objective to be met, the study was required to achieve one of the two primary endpoints. While OCA received breakthrough therapy designation from the FDA in January 2015 for the treatment of NASH patients with liver fibrosis and we currently intend to file for approval of OCA for NASH in the United States and Europe based on the results from the 18-month analysis of our Phase 3 REGENERATE trial in patients with liver fibrosis due to NASH, we do not know if one pivotal clinical trial will be sufficient for marketing approval or if regulatory authorities in the United States, Europe or our other target markets will approve OCA for NASH patients with liver fibrosis on an accelerated or conditional basis, or at all.

Our product candidates may have undesirable side effects which may delay or prevent marketing approval, or, if approval is received, require that our products be taken off the market or include new or additional safety warnings. Any such events may limit our existing and future product sales and materially and adversely affect our business, financial condition and results of operations.

OCA has been shown to be a potent FXR agonist. With the exception of the endogenous human bile acid chenodeoxycholic acid and cholic acid, there are no approved FXR agonists and the adverse effects from long-term exposure to this drug class are unknown. Unforeseen side effects from any of our product candidates, including OCA, could arise either during clinical development or, if approved, after the approved product has been marketed. Serious adverse events, including deaths, in patients taking OCA have occurred in clinical trials and in the post-marketing setting, and we cannot assure you that additional serious adverse events in patients taking OCA in clinical trials or in the post-marketing setting will not occur.

The most common side effects observed in clinical trials of OCA for PBC were pruritus, fatigue, headaches, nausea, constipation and diarrhea. In our Phase 3 POISE trial, pruritus, generally mild to moderate, was the most frequently reported adverse event associated with OCA treatment for PBC and was observed in

38% of patients on placebo, 70% of patients in the OCA 10 mg group and 56% of patients in the OCA titration group (5 mg to 10 mg). Eight patients discontinued due to pruritus, of whom none were in the placebo group, seven (10%) were in the OCA 10 mg group and one (1%) was in the OCA titration group. Pruritus also has been observed in other clinical trials of OCA. Decreases in HDL cholesterol were also observed during treatment in our Phase 3 POISE trial. In our Phase 2 trials for OCA for PBC, a dose-response relationship was observed in the occurrence of liver-related adverse reactions, including jaundice, ascites and primary biliary cholangitis flare with dosages of OCA of 10 mg once daily to 50 mg once daily (up to 5-times the highest recommended dosage), as early as one month after starting treatment with OCA. The European label for Ocaliva also notes that elevations in alanine amino transferase and aspartate aminotransferase were observed in patients treated with OCA.

In the course of our post-marketing pharmacovigilance activities, deaths have been reported in PBC patients with moderate or severe hepatic impairment. In an analysis performed by us and in consultation with the FDA, we concluded that certain of these patients were prescribed once daily doses of Ocaliva, which is seven times higher than the recommended weekly dose in such patients. As a result, in September 2017, we issued a DHCP letter, and the FDA also subsequently issued its own drug safety communication to reinforce recommended label dosing. Both communications remind healthcare providers of the importance of the recommended reduced dosing of Ocaliva in PBC patients with moderate or severe hepatic impairment, while reiterating the importance of monitoring PBC patients for progression of their disease and the occurrence of liver-related adverse reactions. In addition to the DHCP letter, we took actions to enhance education about appropriate use of Ocaliva. These initiatives included: reeducating physicians on the label, with a focus on ensuring appropriate dosing for patients with moderate or severe hepatic impairment; enhancing monitoring of patients for liver-related adverse reactions; and adjudicating reported cases of serious liver injury, including in patients with no or mild hepatic impairment. In February 2018, we announced that the Ocaliva label in the United States had been updated by the FDA to include a boxed warning and a dosing table that reinforced the then-existing dosing schedule for patients with Child-Pugh Class B or C or decompensated cirrhosis. In addition, the FDA issued an updated drug safety communication to accompany the revised label. We remain focused on the safety of all of the patients using Ocaliva within and outside of our ongoing clinical studies and have engaged with relevant regulatory authorities to ensure that the Ocaliva label sufficiently reinforces the importance of appropriate dosing in patients with advanced cirrhosis. These events and any safety concerns associated with Ocaliva, perceived or real, may adversely affect the successful development and commercialization of our product candidates and lead to a loss of revenues.

Ocaliva is contraindicated for PBC patients with complete biliary obstruction in the United States and the European Union. For PBC patients with HDL reductions and no response to Ocaliva after one year at the maximum tolerated dose, the U.S. label asks prescribing physicians to weigh the risks against the benefits of continuing treatment.

In the 18-month analysis of our pivotal Phase 3 REGENERATE trial in patients with liver fibrosis due to NASH, the safety population included 1,968 randomized patients who received at least one dose of investigational product (OCA or placebo). Adverse events were generally mild to moderate in severity and the most common were consistent with the known profile of OCA. The frequency of serious adverse events was similar across treatment arms (11% in placebo, 11% in OCA 10 mg and 14% in OCA 25 mg) and no serious adverse event occurred in > 1% of patients in any treatment arm. There were 3 deaths in the study (2 in placebo: bone cancer and cardiac arrest, 1 in OCA 25 mg: glioblastoma) and none were considered related to treatment. The most common adverse event reported was dose-related pruritus (19% in placebo, 28% in OCA 10 mg and 51% in OCA 25 mg). The large majority of pruritus events were mild to moderate, with severe pruritus occurring in a small number of patients (< 1% in placebo, < 1% in OCA 10 mg and 5% in OCA 25 mg). A higher incidence of pruritus associated treatment discontinuation was observed for OCA 25 mg (< 1% in placebo, < 1% in OCA 10 mg and 9% in OCA 25 mg). According to the clinical study protocol, investigator assessed severe pruritus mandated treatment discontinuation. Consistent with observations from previous NASH studies, OCA treatment was associated with an increase in LDL cholesterol, with a peak increase of 22.6 mg/dL at 4 weeks and subsequently reversing and approaching baseline at month 18 (4.0 mg/dL increase from baseline). Triglycerides rapidly and continually decreased in the OCA treatment arms through month 18. There were few and varied serious cardiovascular events and incidence was balanced

across the three treatment arms (2% in placebo, 1% in OCA 10 mg and 2% in OCA 25 mg). With respect to hepatobiliary events, more patients (3%) on OCA 25 mg experienced gallstones or cholecystitis compared to < 1% on placebo and 1% on OCA 10 mg. While numerically higher in the OCA 25 mg treatment arm, serious hepatic adverse events were uncommon with < 1% incidence in each of the three treatment arms.

In the Phase 2b FLINT trial, pruritus occurred more frequently in the OCA treatment group than in the placebo treatment group (23% vs. 6%, $p < 0.0001$) and at a higher grade (predominately moderate pruritus). OCA treatment was also associated with changes in serum lipid levels, including increases in total cholesterol and LDL cholesterol and a decrease in HDL cholesterol, that were observed within 12 weeks of initiating treatment, peaked and then decreased in magnitude while on treatment, and reversed further during the 24-week post-treatment period. These changes in cholesterol levels, along with the achievement of pre-defined efficacy criteria, played a role in the decision of the FLINT data and safety monitoring board to terminate the treatment phase of the Phase 2b FLINT trial, and the publication of the FLINT results noted the need for further study of these changes. There were two patient deaths in the Phase 2b FLINT trial, and neither death was considered related to OCA treatment.

In December 2015, we initiated a Phase 2 clinical trial, known as the CONTROL trial, to characterize the lipid metabolic effects of OCA and cholesterol management effects of concomitant statin administration in NASH patients. CONTROL enrolled 80 NASH patients who were naïve to statin therapy or had undergone a statin washout period. The study included a 16-week double-blind phase followed by an optional LTSE phase of the trial. OCA treatment in the absence of statin therapy over the first four weeks resulted in an increase in LDL across all OCA treatment groups, while the placebo group was relatively unchanged. Treatment with atorvastatin beginning at week four and continuing through week 16 reversed OCA-related increases in LDL to below baseline levels in all OCA treatment groups. Dose-dependent pruritus was the most common adverse event in patients treated with OCA, occurring in 5% of patients on placebo, 5% of patients in the OCA 5 mg group, 10% of patients in the OCA 10 mg group and 55% of patients in the OCA 25 mg group. All adverse events were mild to moderate and two patients discontinued treatment in the OCA 25 mg group due to pruritus. Over 95% of the patients completing the double-blind phase of CONTROL enrolled in the LTSE phase of the trial.

During the LTSE phase of CONTROL, there was one patient death. This patient was a 64 year-old male with a history of NASH associated liver cirrhosis, morbid obesity (BMI >40) and type 2 diabetes. At baseline, this patient had blood tests consistent with impaired liver function (e.g., low LDL and low platelets). The patient was randomized to placebo for the double-blind phase of the study. Early in the double-blind phase, the patient had serum biochemistry changes consistent with worsening hepatic impairment (e.g., albumin decline and bilirubin was increasing). Atorvastatin was started per protocol and then stopped early due to the patient's persistently low LDL levels. The patient later enrolled in the LTSE phase and began receiving OCA 25 mg treatment. Over the following four months, the patient's serum biochemistry remained consistent with ongoing hepatic impairment. Approximately five months after starting the LTSE phase, the patient developed severe protracted diarrhea, which resulted in weight loss of 30 pounds over the ensuing one-month period. Both an infectious cause and possible inflammatory bowel disease were suspected, and the patient subsequently was started on broad spectrum antibiotics and steroid therapy. Due to the diarrhea, the principal investigator stopped treatment with OCA and discontinued the patient from the study. Concurrently, the patient reported jaundice and was found to have significantly elevated serum bilirubin and ALP, while other liver enzymes remained relatively stable. Over the ensuing two-week period, various diagnostic tests and procedures were performed (e.g., magnetic resonance cholangiopancreatography to investigate possible gallstone bile duct obstruction) and the patient continued receiving a number of other medications, including the ongoing course of steroid therapy. During this time, the patient continued to deteriorate and was hospitalized with acute renal and liver failure, complicated by severe metabolic acidosis. The patient rapidly progressed to multi-organ system failure, sepsis and death.

The principal investigator determined that the events leading to the patient's death were unlikely related to OCA. Despite the numerous confounding factors in this case, given the contemporaneous administration of OCA during the patient's ongoing deterioration, we determined that it could not be ruled out that these events

were possibly related to treatment. Subsequent to our determination, the independent data safety monitoring committee separately evaluated the case and determined that the events leading to the patient's death were unlikely related to OCA.

In our Phase 2 AESOP trial of OCA for PSC, pruritus was the most common adverse event, occurring in 46% of patients on placebo, 60% of patients in the OCA 1.5 mg to 3 mg group and 67% of patients in the OCA 5 mg to 10 mg group, with the severity increasing with dose. One (4%) patient in the OCA 1.5 mg to 3 mg group and three (12%) patients in the OCA 5 mg to 10 mg group discontinued OCA due to pruritus compared to none in the placebo group.

Additional or unforeseen side effects relating to OCA or any of our other product candidates could arise either during clinical development or, if approved, after the approved product has been marketed. With the approval of Ocaliva for PBC in the United States, Europe and certain of our other target markets, OCA is currently used in an environment that is less rigorously controlled than in clinical studies. If new side effects are found, if known side effects are shown to be more severe than previously observed or if OCA is shown to have other unexpected characteristics, we may need to abandon our development of OCA for PBC, NASH and other potential indications. Furthermore, our commercial sales of Ocaliva for PBC may be materially and adversely affected.

The range and potential severity of possible side effects from systemic therapies is significant. The results of our current or future clinical trials may show that our product candidates, including OCA, cause undesirable or unacceptable side effects, which could interrupt, delay or halt clinical trials, result in a delay of, or failure to obtain, marketing approval from the FDA and other regulatory authorities, result in marketing approval from the FDA and other regulatory authorities with restrictive label warnings or result in the withdrawal of previously granted marketing approvals.

In addition, our product candidates are being developed as potential treatments for severe, life threatening diseases and, as a result, our trials will necessarily be conducted in patient populations that will be more prone than the general population to exhibit certain disease states or adverse events. For example, our Phase 3 REVERSE trial in NASH patients with compensated cirrhosis has expanded our NASH development program into a more advanced NASH patient population and accordingly imposes certain eligibility requirements for uptitration, as well as certain monitoring requirements thereafter. Ocaliva is prescribed in patients suffering from various stages of PBC, which can be life threatening, and patients may suffer from other concomitant illnesses that may increase the likelihood of certain adverse events. It may be difficult to discern whether certain events or symptoms observed during our clinical trials or by patients using our approved products are related to our product candidates or approved products or some other factor. As a result, we and our development programs may be negatively affected even if such events or symptoms are ultimately determined to be unlikely related to our product candidates or approved products. We cannot assure you that additional or more severe adverse side effects related to OCA or our other product candidates will not be observed in our clinical trials or in the commercial setting. If observed, such adverse side effects could delay or preclude regulatory approval of OCA, limit commercial use or result in the withdrawal of previously granted marketing approvals.

If we or others identify undesirable or unacceptable side effects caused by our product candidates or products:

- we may be required to modify, suspend or terminate our clinical trials;
- we may be required to modify or include additional dosage and administration instructions, warnings and precautions, contraindications, boxed warnings, limitations, restrictions or other statements in the product label for our approved products, or issue field alerts to physicians and pharmacies;
- we may be required to conduct costly additional clinical trials;
- we may be subject to limitations on how we may promote our approved products;
- sales of our approved products may decrease significantly;
- regulatory authorities may require us to take our approved products off the market;

- we may be subject to regulatory investigations, government enforcement actions, litigation or product liability claims; and
- our products may become less competitive or our reputation may suffer.

Breakthrough therapy designation for OCA may not lead to faster development or regulatory processes or increase the likelihood that the FDA will approve OCA for the treatment of NASH patients with fibrosis.

If a drug is intended for the treatment of a serious or life-threatening 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 FDA may grant a breakthrough therapy designation. Breakthrough therapy designation is intended to facilitate the development, and expedite the review, of such drugs, but the breakthrough therapy designation does not assure marketing approval by the FDA.

In January 2015, we received breakthrough therapy designation for OCA for the treatment of NASH patients with fibrosis. However, there is no guarantee that the receipt of breakthrough therapy designation will result in a faster development process, review or approval of OCA for NASH patients with fibrosis or increase the likelihood that OCA will be granted marketing approval for NASH patients with fibrosis. Similarly, any future breakthrough therapy designation relating to any other potential indication of OCA neither guarantees a faster development process, review or approval nor improves the likelihood of the grant of marketing approval by the FDA for any such potential indication of OCA compared to conventional FDA procedures. In addition, the FDA may withdraw any breakthrough therapy designation at any time. While we may seek breakthrough therapy designation for one or more of our other product candidates, we can give no assurance that the FDA will grant such status.

We may not be able to obtain or, if approved, maintain orphan drug exclusivity for our approved products or product candidates, which could cause our revenues to suffer.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs and biologics for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. OCA has received orphan drug designation in the United States and the European Union for the treatment of PBC and PSC.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same product during the exclusivity period. The applicable exclusivity period is seven years in the United States and ten years in Europe. 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 a sufficient quantity of the product to meet the needs of patients with the rare disease or condition. In addition, the European exclusivity period can be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation because, for example, the product is sufficiently profitable not to justify maintenance of market exclusivity.

Any failure to maintain orphan drug status may subject us to mandatory price discounts in Europe and result in the loss of other benefits, such as tax exemptions for sales. As such, the loss of orphan drug status may have a negative effect on our ability to successfully commercialize our products, earn revenues and achieve profitability.

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. Even after an orphan drug is approved, the FDA or EMA may subsequently approve another product for the same condition if the FDA or EMA concludes that the later product is clinically superior (i.e., it is shown to be safer, more effective or makes a major contribution to patient care). Any inability to secure or maintain orphan drug status or the exclusivity benefits of this status could have a material adverse impact on our ability to develop and commercialize our product candidates and approved products.

We rely entirely on third parties for the manufacture of our product requirements for our preclinical studies and clinical trials, as well as our commercial supply of Ocaliva and, if approved, OCA for NASH and our other product candidates, and also depend on third-party vendors and CROs for certain of our clinical trial and product development activities. Our business could be harmed if our third-party manufacturers fail to provide us with sufficient quantities of drug product, or fail to do so at acceptable quality levels or prices, or we lose our relationships with our third-party vendors and CROs and our clinical trial or product development efforts are delayed as a result.

We do not manufacture the pharmaceutical products that we sell or the product candidates that we are developing. We rely on third-party contract manufacturers for all of our required raw materials, API and finished product for our commercial sales and for our existing and anticipated clinical trials and preclinical studies. Any inability by our contract manufacturers to continue to provide services to us for any reason could adversely affect our commercialization efforts and clinical development program, and we may be unable to identify, qualify and engage on terms that are favorable to us replacement suppliers on a timely basis, if at all.

We currently have an agreement with PharmaZell for the manufacture and commercial supply of Ocaliva and, if approved, OCA for NASH. While we have procured supplies for the commercialization of Ocaliva for PBC and, if approved, OCA for NASH, we may not be able to procure sufficient supplies of Ocaliva and, if approved, OCA for NASH on an ongoing basis. We have engaged in activities to qualify additional or back-up suppliers, but these suppliers may not be able to meet our long-term commercial supply requirements for Ocaliva or, if approved, OCA for NASH or other indications on acceptable terms, or at all. We do not have agreements for long-term supplies of any of our other product candidates. We currently obtain supplies and services relating to our other product candidates from our third-party contract manufacturers on a purchase order basis.

The facilities used by any contract manufacturer to manufacture OCA or any of our other product candidates must be the subject of a satisfactory inspection before the FDA or regulators in other jurisdictions approve the product candidate manufactured at that facility. We are completely dependent on these third-party manufacturers for compliance with the requirements of U.S. and non-U.S. regulators for the manufacture of our finished products, including Ocaliva. If our manufacturers are unable to meet our requirements in accordance with our product specifications and applicable cGMP requirements, our products or product candidates will not be approved or, if already approved, may be subject to recall.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured our product candidates and products ourselves, including:

- the possibility that we are unable to enter into or renew our manufacturing agreements with third parties on acceptable terms, or at all;
- the possible termination or breach by our third-party manufacturers of our manufacturing agreements based on factors beyond our control; and
- our inability to timely identify and qualify a replacement for any of our third-party manufacturers in the event any such third-party manufacturer fails to meet our product requirements or following the termination, expiration or nonrenewal of our agreements with such third-party manufacturer.

Any of these factors could disrupt the supply of our product candidates or approved products, cause us to incur higher costs, delay the approval of our product candidates or prevent or disrupt the commercialization of our approved products. Furthermore, if any of our product candidates, including OCA for NASH, are approved and our contract manufacturers fail to deliver the required commercial quantities of finished product on a timely basis and at commercially reasonable prices and we are unable to find one or more replacement manufacturers capable of production at a substantially equivalent cost, in substantially equivalent volumes and quality and on a timely basis, we would likely be unable to meet demand for such product candidate following its approval and could lose potential revenue. It may take several years to establish an alternative long-term source of supply and to have any such new source approved by the regulatory authorities that regulate our products in the United States, Europe and our other target markets.

We depend on third-party vendors and CROs for certain of our clinical trial and product development activities. If we are unable to maintain our relationship with any one or more of these providers, we could experience a significant delay in both identifying another comparable provider and then contracting for its services, which could adversely affect our clinical trial and product development efforts. We may be unable to retain an alternative provider on reasonable terms, or at all. Even if we locate an alternative provider, it is likely that such a provider will need additional time to respond to our needs and may not provide the same type or level of services as the original provider. In addition, any CRO that we retain will be subject to the FDA's regulatory requirements and similar foreign standards and we do not have control over compliance with these regulations by these providers. If these requirements and standards are not adhered to by these providers, the commercialization and development of our product candidates or approved products could be delayed, which could harm our business and financial condition.

Even though we have received conditional approval of Ocaliva for PBC, we and our contract manufacturers are still subject to strict, ongoing regulatory requirements.

Even though we have received conditional approval of Ocaliva for the treatment of PBC in combination with UDCA in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA, we and our contract manufacturers are subject to ongoing regulatory requirements relating to, among other things, Ocaliva's manufacturing, labeling, packaging and storage. In addition, we and our contract manufacturers and our contract manufacturers' facilities are required to comply with extensive FDA and EMA requirements and the requirements of other similar regulatory authorities, including requirements that quality control and manufacturing procedures conform to current cGMPs. As such, we and our contract manufacturers are subject to periodic cGMP inspections and must continue to expend time, money and effort to ensure compliance with applicable manufacturing, production and quality control requirements. We are also required to report certain adverse reactions and production problems, if any, to the FDA, EMA and other similar regulatory authorities and to comply with certain requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and generally must be consistent with the information in the product's approved label.

If a regulatory authority such as the FDA discovers previously unknown problems with one of our products, such as adverse events of unanticipated severity or frequency or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of one of our products, it may impose restrictions on that product or us, including requiring withdrawal of the product from the market. In addition, if we or our contract manufacturers, other third-party vendors or collaborators fail to comply with applicable regulatory requirements, a regulatory agency may, among other things:

- issue Form 483 notices or Warning Letters, in the case of the FDA, or similar notices, in the case of other regulatory agencies;
- mandate modifications to our promotional materials or require us to provide corrective information to healthcare practitioners;
- require us or our collaborators to enter into a consent decree or permanent injunction, which may include the imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- recall our products;
- suspend any of our ongoing clinical studies;
- impose administrative, civil or criminal penalties;
- withdraw regulatory approval or require changes to our product label, including the inclusion of additional warnings or changes to the approved indication;
- refuse to approve pending applications or supplements to approved applications filed by us or our collaborators;

- impose restrictions on our operations or those of our contract manufacturers, including costly new manufacturing requirements; or
- seize or detain products.

We must comply with environmental, health and safety laws and regulations

Our activities involve the controlled storage, use and disposal of hazardous materials. We are subject to federal, state, city and local laws and regulations, in and outside the United States, governing the use, manufacture, storage, handling and disposal of these hazardous materials. Although we believe that the safety procedures we use for handling and disposing of these materials comply with the standards prescribed by applicable laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, regulatory authorities may curtail the use of these materials and interrupt our business operations. We do not currently maintain hazardous materials insurance coverage.

Risks Related to the Commercialization of Our Products

Sales of Ocaliva may be adversely affected by safety and labeling changes required by the FDA.

In the course of our post-marketing pharmacovigilance activities, deaths have been reported in PBC patients with moderate or severe hepatic impairment. In an analysis performed by us and in consultation with the FDA, we concluded that certain of these patients were prescribed once daily doses of Ocaliva, which is seven times higher than the recommended weekly dose in such patients. As a result, in September 2017, we issued a DHCP letter and the FDA also subsequently issued its own drug safety communication to reinforce recommended label dosing. Both communications remind healthcare providers of the importance of the recommended reduced dosing of Ocaliva in PBC patients with moderate or severe hepatic impairment, while reiterating the importance of monitoring PBC patients for progression of their disease and the occurrence of liver-related adverse reactions. In February 2018, we announced that the Ocaliva label in the United States had been updated by the FDA to include a boxed warning and a dosing table that reinforced the then-existing dosing schedule for patients with Child-Pugh Class B or C or decompensated cirrhosis. In addition, the FDA issued an updated drug safety communication to accompany the revised label. We remain focused on the safety of all of the patients using Ocaliva within and outside of our ongoing clinical studies and have engaged with relevant regulatory authorities to ensure that the Ocaliva label sufficiently reinforces the importance of appropriate dosing in patients with advanced cirrhosis. These events, the revised label, any future label changes that may be required by the FDA or other relevant regulatory authorities and any safety concerns associated with Ocaliva, perceived or real, may adversely affect our Ocaliva commercialization efforts and, consequently, our financial condition and results of operations.

We are subject to uncertainty relating to pricing and reimbursement. Failure to obtain or maintain adequate coverage, pricing and reimbursement for Ocaliva for PBC, OCA for NASH, if approved, or our other future approved products, if any, could have a material adverse impact on our ability to commercialize such products.

The availability and extent of coverage and reimbursement from governmental and private healthcare payors for our products, including Ocaliva for PBC and, if approved, OCA for NASH, and our ability to obtain adequate pricing for such products are key factors that will affect our future commercial prospects. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will cover and establish payment levels. Sales of our products depend and will depend substantially, both domestically and internationally, on the extent to which their cost will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. Accordingly, the coverage and reimbursement decisions of such governmental and private healthcare payors could reduce the demand for, or the price paid for, our products. If these payors do not consider our products to be cost-effective alone, or relative to other approved therapies, they may not cover our products or, if they do, they may apply utilization management restrictions, high patient cost-sharing obligations, or restrict the level of reimbursement.

Third-party payors are increasingly challenging the prices charged for pharmaceuticals products, and many also limit reimbursement for newly-approved products and indications. Third-party payors often attempt

to contain healthcare costs by demanding price discounts or rebates and limiting both the types and variety of drugs that they will cover and the amounts that they will pay for drugs. As a result, they may not provide adequate payment for our products. Similarly, the containment of healthcare costs has become a priority for federal and state governments and the pricing of pharmaceutical products has been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could adversely affect our ability to successfully commercialize our products. In addition, we may be required to conduct post-marketing studies in order to demonstrate the cost-effectiveness of our products to payors' satisfaction. Such studies might require us to commit a significant amount of management's time and our financial and other resources and our products might not ultimately be considered cost-effective.

We do not know if Ocaliva for PBC will obtain and maintain broad acceptance from third-party payors in the jurisdictions in which it is, or may in the future be, approved. In addition, we do not know if OCA for NASH will obtain and maintain broad acceptance from third-party payors, if approved. The coverage determination process is a time-consuming and costly process that requires us to provide scientific and clinical support for the use of Ocaliva for PBC and, if approved, OCA for NASH to each payor separately, with no assurance that coverage will be obtained or maintained. The market for a drug depends significantly on access to third-party payors' drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement. Third-party payors may refuse to include a particular drug in their formularies or restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available, even if not approved for the indication for which the branded drug is approved. Due to there being no uniform policy of coverage and reimbursement in the United States among commercial payors, coverage and reimbursement for pharmaceutical products may differ significantly from payor to payor. If we are unable to obtain and maintain adequate coverage from third-party payors, the adoption of Ocaliva for PBC and, if approved, OCA for NASH by physicians and patients may be limited. This in turn could affect our ability to successfully commercialize Ocaliva for PBC and, if approved, OCA for NASH and have a material adverse impact our profitability, results of operations, financial condition and future success.

We cannot be certain that we will be able to obtain and maintain adequate coverage, pricing and reimbursement for our products, including Ocaliva for PBC, OCA for NASH, if approved, or our other future approved products, if any. If coverage or reimbursement is not available or is available on a limited basis, or if we are unable to obtain and maintain adequate pricing, we may not be able to successfully commercialize Ocaliva for PBC, OCA for NASH, if approved, or our other future approved products, if any.

Legislative healthcare reform may adversely affect our business.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (the ''MMA'') changed the way Medicare covers and pays for pharmaceutical products. The legislation established Medicare Part D, which expanded Medicare coverage for outpatient prescription drug purchases by the elderly but provided authority for limiting the number of drugs that will be covered in any therapeutic class. The MMA also introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. Any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act (collectively, the ''ACA''), became law in the United States. Among other things, the purpose of the ACA was to reduce the cost of healthcare and substantially change the way healthcare is financed by both governmental and private insurers. The ACA requires discounts under the Medicare drug benefit program and increased the rebates paid by pharmaceutical companies on drugs covered by Medicaid. The ACA also imposes an annual fee, which increases each year, on sales by branded pharmaceutical manufacturers. Since its enactment, there have been a number of judicial, executive and legislative challenges to the ACA, including recent tax legislation that removes the financial penalties for

people who do not carry health insurance commencing in 2019 and an Executive Order signed in October 2017 by President Trump directing federal agencies to modify how the ACA is implemented. There is still uncertainty whether the ACA will undergo additional revisions, and we cannot predict the impact of any future modifications. There have also been recent state legislative efforts to address drug costs, which have generally focused on increasing transparency around drug costs or limiting drug prices. We cannot predict the success of any such current or future federal or state legislative efforts.

Reimbursement in the European Union and many other territories must be negotiated on a country-by-country basis and in many countries a product cannot be commercially launched until reimbursement is approved. The timing to complete the negotiation process in each country is highly uncertain. Even after a price is negotiated, countries frequently request or require adjustments to the price and other concessions over time or require approvals regionally. Reimbursement agencies in Europe are often more conservative than those in the United States and the reimbursement process is often slower since reimbursement decisions are made on a country-by-country basis. Prices for drugs in Europe are generally lower than in the United States and tend to decrease over time.

The United States and several other jurisdictions are considering, or have already enacted, a number of legislative and regulatory proposals to change their healthcare systems in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. We expect to experience pricing pressures in connection with the sale of Ocaliva and our other future approved products, if any, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals. Pricing pressures recently experienced by the pharmaceutical industry may be further exacerbated by legislative and policy changes under consideration by the Trump administration.

Ocaliva and our other future approved products, if any, may not achieve broad market acceptance among physicians, patients and healthcare payors, and revenues generated from their sales may be limited as a result.

The commercial success of Ocaliva for PBC, OCA for NASH, if approved, and our other future approved products, if any, will depend upon their acceptance among the medical community, including physicians, healthcare payors and patients. In order for Ocaliva to be commercially successful for PBC, we need to demonstrate its utility as a cost-effective treatment for PBC patients who have an inadequate response to UDCA or who are unable to tolerate UDCA. Ocaliva also must be shown to be a safe and tolerable treatment in a commercial use setting as it is intended to be a lifetime therapy for patients eligible for treatment. We cannot be certain that Ocaliva for PBC, OCA for NASH, if approved, or our other future approved products, if any, will achieve an adequate level of acceptance among the medical community, including physicians, healthcare payors and patients.

The degree of market acceptance of our approved products depends on a number of factors, including:

- limitations, warnings, precautions, boxed warnings, contraindications, restrictions or other statements contained in the product label approved by the FDA, EMA or other relevant regulatory authorities;
- changes in the standard of care or availability of alternative therapies at similar or lower costs for the targeted indications for any of our products, such as UDCA for the treatment of PBC;
- limitations in the approved indications for our products;
- demonstrated clinical safety and efficacy compared to other products;
- a lack of adverse side effects, including deaths and other serious adverse events;
- sales, marketing and distribution support;
- the availability of reimbursement from managed care plans and other third-party payors;
- the timing of the market introduction and perceived safety and efficacy of competitive products;

- the degree of cost-effectiveness;
- availability of alternative therapies at similar or lower cost, including generics and over-the-counter products;
- the extent to which our products are approved for inclusion on formularies of hospitals and managed care organizations;
- whether and to what extent our products are recommended under physician treatment guidelines for the treatment of the indications for which we have received regulatory approval;
- adverse publicity about our products or favorable publicity about competitive products;
- the convenience and ease of administration of our products; and
- potential product liability claims.

In addition, the potential market opportunity for Ocaliva for PBC, OCA for NASH, if approved, and our other future approved products, if any, is difficult to precisely estimate. For example, our estimates of the potential market opportunity for Ocaliva for PBC include a number of key assumptions related to prevalence rates, patients' access to healthcare, diagnosis rates and patients' response to or tolerance of Ocaliva, which are based on available literature and epidemiology research in PBC, our industry knowledge gained through market research and other methods, industry publications, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions. If any of these assumptions prove to be inaccurate, then the actual market for Ocaliva for PBC could be smaller than our estimates of our potential market opportunity. If the actual market opportunity for Ocaliva for PBC, OCA for NASH, if approved, or our other future approved products, if any, is smaller than we expect, our product revenue may be limited and our financial condition and results of operations may be materially adversely affected.

If Ocaliva for PBC, OCA for NASH, if approved, or our other future approved products, if any, do not achieve an adequate level of acceptance among the medical community, including physicians, healthcare payors and patients, sufficient revenue may not be generated from these products and we may not become or remain profitable. In addition, our efforts to educate the medical community and third-party payors on the benefits of Ocaliva for PBC, OCA for NASH, if approved, and our other future approved products, if any, may require significant resources and may never be successful.

We have limited sales, marketing and distribution experience and we will need to continue to invest in significant additional resources to develop those capabilities or enter into acceptable third-party sales and marketing arrangements.

We have limited sales, marketing and distribution experience as a commercial organization. Ocaliva is our first approved product and the commercial launch of Ocaliva for PBC is our first product launch. We are commercializing Ocaliva for PBC using a combination of our internal commercial organization, a contract sales organization and third-party distributors depending on the jurisdiction. We are developing our commercialization strategy for OCA for NASH, if approved, and have not yet decided on our commercialization strategy for OCA for other indications or for our other product candidates, in each case, if approved. To develop internal sales, distribution and marketing capabilities, we have invested and expect to continue to invest significant additional amounts of financial and management resources.

Recruiting and training a commercial organization is expensive, time-consuming and could delay any product launch. If the commercial launch of an approved product for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment could be lost if we cannot retain or reposition our sales and marketing personnel.

For approved products where we decide to perform sales, marketing and distribution functions ourselves or through third parties, we could face a number of additional risks, including:

- we or our third-party sales collaborators may not be able to attract and build, or retain, an effective marketing or sales force;

- the cost of securing or establishing a marketing or sales force may exceed the revenues generated by any products; and
- our sales and marketing efforts may not be successful.

Sumitomo Dainippon has an exclusive license to develop and commercialize OCA for the treatment of PBC and NASH in China (excluding Taiwan), and we may utilize the services of third-party collaborators in certain other jurisdictions. We may have limited or no control over the sales, marketing and distribution activities of these third parties, and our future revenues may depend heavily on their success.

We could incur significant liability if it is determined that we have improperly promoted or are improperly promoting Ocaliva for PBC or any of our product candidates prior to their approval.

Physicians are permitted to prescribe drug products for uses that are not described in the product's labeling and that differ from those approved by the FDA or other applicable regulatory agencies. Off-label uses are common across medical specialties. Although the FDA and other regulatory agencies do not regulate a physician's choice of treatments, the FDA and other regulatory agencies do restrict communications on the subject of off-label use. Companies are not permitted to promote drugs in a manner inconsistent with applicable regulatory guidance. The FDA, the U.S. Department of Justice (''DOJ'') and other regulatory and enforcement authorities actively enforce laws and regulations prohibiting the improper promotion of approved products, as well as the promotion of products for which marketing approval has not been obtained. A company that is found to have improperly promoted off-label uses will be subject to significant liability, including civil and administrative remedies as well as criminal sanctions. A significant number of pharmaceutical companies have received inquiries or been the subject of investigations by various governmental authorities in the United States and abroad. For example, in May 2018, we received a subpoena from the SEC requesting information in connection with our patient assistance program and certain of our commercial activities, and in August 2018, we received an inquiry from the DOJ requesting the voluntary production of certain information regarding the Company's activities and public statements concerning Ocaliva's dosing, use, adverse events, marketing and reimbursement.

While we have implemented a corporate compliance program based on what we believe are current best practices, we cannot provide any assurance that governmental authorities, including the DOJ, SEC or FDA, will find that our business practices comply with all current or future administrative or judicial interpretations of potentially applicable laws and regulations. In addition, government and regulatory agencies may hold us responsible for any actions by our sales representatives or sales organizations, including our contract sales organization, to the extent that they do not comply with applicable laws and regulations. If we or our contract sales organization fail to comply with any of these laws and regulations, we could be subject to a range of penalties, including criminal and significant civil penalties, fines, damages, curtailment or restructuring of our operations, exclusion, disqualification or debarment from participation in federally- or state-funded healthcare programs or other sanctions or litigation, any of which could have a material adverse impact on our business, financial condition and results of operations.

If we market products in a manner that violates healthcare fraud and abuse laws, or if we violate government price reporting or physician payment disclosure laws, we may be subject to civil or criminal penalties.

In addition to FDA restrictions on the marketing of pharmaceutical products, several other types of state and federal healthcare laws, commonly referred to as ''fraud and abuse'' laws, have been applied in recent years to restrict certain marketing practices in the pharmaceutical industry. Other jurisdictions including Europe have similar laws and are enacting more stringent regulations. These laws include false claims and anti-kickback statutes. If we market our products and our products are paid for by governmental programs, it is possible that some of our business activities could be subject to challenge under one or more of these laws.

Federal false claims laws generally prohibit anyone from knowingly and willingly presenting, or causing to be presented, any claims for the payment for goods (including drugs) or services to third-party payers (including Medicare and Medicaid) that are false or fraudulent. The federal civil monetary penalties statute, likewise, imposes penalties against any person or entity that, among other things, is determined to have

presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to generate business, including the purchase or prescription of a particular product covered by Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers or formulary managers on the other. Although there are several statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exemption or safe harbor. In addition, such exemptions and safe harbors are subject to change from time to time. For example, in January 2019, the U.S. Department of Health and Human Services issued a proposed rule that, if finalized, would modify the discount safe harbor under the federal anti-kickback statute to eliminate protection for certain drug discounts paid by manufacturers to plan sponsors under Medicare Part D or Medicaid managed care organizations or the pharmacy benefit managers working with these organizations.

HIPAA created additional federal criminal statutes that prohibit, among other things, 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, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. HIPAA also imposes significant requirements on the receipt and transfer of protected health information.

In addition, the federal transparency requirements under the Physician Payments Sunshine Act require certain manufacturers of drugs, including us, for which payment is available under certain federal healthcare programs annually to report information related to payments and other transfers of value to physicians and teaching hospitals, and physician ownership and investment interests.

Finally, we must offer discounted pricing or rebates on Ocaliva under various federal and state healthcare programs, and report specific prices to government agencies under healthcare programs. The calculations necessary to determine the prices reported are complex and the failure to report prices accurately may expose us to significant penalties.

There are foreign and state law equivalents of these laws and regulations, such as anti-kickback, false claims, transparency and data privacy and security laws, to which we are currently and/or may in the future be subject. We may also be subject to foreign and state laws that require manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. Many of these laws differ from each other in significant ways, thus increasing the cost and complexity of our compliance efforts.

A number of pharmaceutical and other healthcare companies have been prosecuted under these laws for a variety of promotional and marketing activities, including providing free trips, free goods, sham consulting fees and grants and other monetary benefits to prescribers; reporting inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in improper promotional activities; and submitting inflated best price information to the Medicaid Rebate Program to reduce liability for Medicaid rebates.

If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including criminal and significant civil penalties, damages, fines, imprisonment, exclusion of products from reimbursement under United States federal or state healthcare programs, and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could materially adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action

against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with these laws may prove costly.

We may not be successful in establishing, implementing and maintaining development and commercialization collaborations, which could adversely affect our ability to develop certain of our product candidates and our financial condition and operating results. If any strategic collaborator fails to perform its obligations under, or terminates, its agreement with us, our business could be substantially harmed.

Developing pharmaceutical products, conducting clinical trials, obtaining regulatory approval, expanding manufacturing capabilities and marketing approved products are expensive, complex and time-consuming undertakings. As a result, we have in the past entered into, and may in the future seek to enter into, collaborations with third parties upon whom we may rely for financial resources and for development, regulatory and commercialization expertise for selected products or product candidates and in selected jurisdictions. For example, Sumitomo Dainippon has an exclusive license to develop and commercialize OCA for the treatment of PBC and NASH in China (excluding Taiwan). We may also establish collaborations with respect to the development and commercialization of OCA in other jurisdictions and for our other product candidates. Additionally, we may enter into sales and marketing arrangements with third parties with respect to our approved products in all or certain jurisdictions.

Our collaborators may fail to develop or effectively commercialize products, product candidates or technologies for a variety of reasons, including a lack of sufficient resources, a decision not to devote the necessary resources due to internal constraints, such as limited cash or human resources, a change in strategic focus or a failure to obtain the necessary regulatory approvals. For example, our strategic collaboration with Sumitomo Dainippon may not be successful due to a number of important factors, including the following:

- Sumitomo Dainippon has significant discretion in determining the efforts and resources that it will apply to its strategic collaboration with us. The timing and amount of any cash payments, milestones and royalties that we may receive will depend on, among other things, the efforts, allocation of resources and successful development and, if approved, commercialization of OCA in China (excluding Taiwan) by Sumitomo Dainippon;
- subject to certain restrictions contained in our license agreement, it is possible that Sumitomo Dainippon may develop and commercialize, either alone or with others, or be acquired by a company that has, products that are similar to or competitive with the product candidates that it licenses from us;
- Sumitomo Dainippon may change the focus of its development and commercialization efforts or pursue higher-priority programs;
- Sumitomo Dainippon may, under specified circumstances, terminate our license agreement on short notice and for circumstances outside of our control, which could make it difficult for us to attract new strategic collaborators or adversely affect how we are perceived in the scientific and financial communities;
- Sumitomo Dainippon has, under certain circumstances, the right to maintain or defend our intellectual property licensed to it in its territory and, although we may have the right to assume the maintenance and defense of our intellectual property if Sumitomo Dainippon does not, our ability to do so may be compromised by its acts or omissions;
- Sumitomo Dainippon may utilize our intellectual property in such a way as to invite litigation that could jeopardize our intellectual property or expose us to potential liability; and
- Sumitomo Dainippon may not comply with all applicable regulatory requirements.

We and Sumitomo Dainippon have agreed that if certain clinical development milestones in China (excluding Taiwan) are not met by December 31, 2020, Sumitomo Dainippon may choose either to pay us a milestone payment or terminate our license agreement. Sumitomo Dainippon may also terminate the Sumitomo Agreement in its entirety or on an indication-by-indication basis at any time upon 90 days' written notice. If Sumitomo Dainippon fails to develop or effectively commercialize OCA for PBC or NASH in China

(excluding Taiwan), or terminates our license agreement, we may not be able to replace it with another collaborator. Sumitomo Dainippon has returned the rights to develop and commercialize OCA in Japan and Korea and we agreed to forego any further milestone or royalty payments with respect thereto. We may not be successful in reaching an agreement with an alternative collaborator for Japan and Korea.

If we are unable to maintain our existing arrangements or enter into new arrangements on acceptable terms, or at all, we may be unable to effectively market and sell our products in certain of our target markets. We expect to face competition in seeking appropriate collaborators. Moreover, collaboration and similar arrangements are complex and time consuming to negotiate, document and implement and they may require substantial resources to maintain. We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements for the development of our product candidates. When we collaborate with a third party for development and commercialization of a product candidate or approved product, we expect to relinquish some or all of the control over the future success of that product candidate or approved product to the third party. Our collaboration partner may not devote sufficient resources to the commercialization of our approved products or may otherwise fail in their commercialization. The terms of any collaboration or other arrangement that we establish may not be favorable to us. In addition, any collaboration that we enter into may be unsuccessful. In some cases, we may be responsible for continuing preclinical and initial clinical development of a partnered product candidate or research program, and the payment we receive from our collaboration partner may be insufficient to cover the cost of this development. If we are unable to reach agreements with suitable collaborators, we may incur increased costs and we may be forced to limit the number of products or product candidates we can commercially develop or the territories in which we can commercialize them. If we fail to achieve successful collaborations, our operating results and financial condition could be materially and adversely affected.

If we fail to develop OCA for additional indications such as NASH, our commercial opportunity will be limited.

To date, we have focused the majority of our development efforts on the development of OCA. One of our strategies is to pursue clinical development of OCA for NASH and other progressive non-viral liver diseases, to the extent that we have sufficient funding to do so.

PBC is an orphan disease and the potential market size for Ocaliva for PBC is relatively limited. Furthermore, because a significant proportion of PBC patients do not exhibit any symptoms at the time of diagnosis, PBC may be left undiagnosed for a significant period of time. Due to these factors, our ability to grow revenues will be dependent on our ability to increase market share and successfully develop and commercialize OCA for the treatment of additional indications. In particular, we believe that our future success will depend in large part on the results of our development of OCA for the treatment of NASH. Although NASH is believed to be one of the most prevalent chronic liver diseases worldwide, NASH may be left undiagnosed in patients for a long period of time and a definitive diagnosis of NASH is currently based on a histological assessment of a liver biopsy, which impacts the ability to easily identify patients. Furthermore, even if we are successful in developing and obtaining marketing approval of OCA for the treatment of NASH, we may not be able to successfully commercialize OCA for NASH.

The completion of development, securing of approval and commercialization of OCA for additional indications such as NASH will require substantial additional funding and is prone to the risks of failure inherent in drug development. We cannot provide you any assurance that we will be able to successfully advance any of these indications through the development process. Even if we receive regulatory approval to market OCA for the treatment of NASH or any other additional indications, we cannot assure you that any such additional indications will 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 OCA for NASH or other additional indications, our commercial opportunity will be limited and our business prospects will suffer.

Risks Related to Our Business and Strategy

We depend on third-party contractors for a substantial portion of our operations and may not be able to control their work as effectively as if we performed these functions ourselves.

We outsource and plan to continue to outsource substantial portions of our operations to third-party service providers, including CROs for certain of our clinical trial and product development activities, contract manufacturers for the production of active pharmaceutical ingredient and finished drug product for our commercial sales and for our clinical trials and preclinical studies and a contract sales organization for the commercialization of Ocaliva in certain jurisdictions. We will likely also use the services of third-party vendors in connection with our future commercialization activities, including product sales, marketing and distribution. Our agreements with third-party service providers are on a study-by-study and/or project-by-project basis. Typically, we may terminate these agreements with notice and are responsible for the supplier's previously incurred costs. In addition, a number of third-party service providers that we retain will be subject to the FDA's and EMA's regulatory requirements and similar standards outside of the United States and Europe and we do not have control over compliance with these regulations by these providers. If these providers do not adhere to applicable governing practices and standards, the development and commercialization of Ocaliva and our product candidates could be delayed or stopped, which could severely harm our business and financial condition.

Because we have relied on third parties, our internal capacity to perform these functions is limited. Outsourcing these functions involves the risk that third parties may not perform to our standards, may not produce results in a timely manner or may fail to perform at all. In the past, we experienced difficulties with a third-party contract manufacturer for OCA, including delays in receiving adequate clinical trial supplies as and when requested. We subsequently replaced this manufacturer, but it is possible that we could experience similar difficulties in the future. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated. There are a limited number of third-party service providers that have the specialized expertise required to achieve our business objectives. Identifying, qualifying and managing the performance of third-party service providers can be difficult, time-consuming and cause delays in our development programs. Despite our growth, we have limited internal resources available to identify and monitor third-party service providers. To the extent we are unable to identify, retain and successfully manage the performance of third-party service providers, our business may be materially adversely affected. We may further be subject to the imposition of civil or criminal penalties if their conduct violates applicable law.

Our third-party service providers generally are not prohibited from providing their services to other biopharmaceutical companies, including companies that currently or may in the future compete with us. For example, certain of our third-party service providers and consultants may be able to develop intellectual property to which we are not entitled under our agreements and that may eventually be used to develop products that compete with our products. Although we generally have confidentiality and non-disclosure agreements in place with our third-party service providers and consultants, such third parties may be able to provide services to other companies without violating the terms of our agreements. In addition, although we may seek to enter into non-compete arrangements with our key third-party service providers, such arrangements are difficult to negotiate and we may be unable to successfully enter into such arrangements.

We face rapid technological change and competition from other biotechnology and pharmaceutical companies. Our operating results will suffer if we fail to compete effectively.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We have competitors in the United States, Europe and other jurisdictions, including major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical and generic drug companies and universities and other research institutions. Many of our competitors have financial, sales and marketing, manufacturing and distribution, legal, regulatory and product development resources substantially greater than ours. Large pharmaceutical companies, in particular, have extensive experience in research, clinical testing, obtaining regulatory approvals, recruiting patients and manufacturing pharmaceutical products. These companies also have significantly greater sales and marketing capabilities and often have collaborative arrangements in our target markets. Established pharmaceutical

companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make our products or product candidates obsolete. As a result of all of these factors, our competitors may succeed in obtaining patent protection and/or FDA, EMA or other regulatory approval or discovering, developing and commercializing drugs for the diseases that we are targeting before we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies.

Some of the pharmaceutical and biotechnology companies that we expect to compete with include Allergan plc, Acorda Therapeutics, Inc., Arena Pharmaceuticals, Inc., AstraZeneca plc, Boehringer Ingelheim GmbH, Bristol-Myers Squibb Company, Conatus Pharmaceuticals Inc., CymaBay Therapeutics, Inc., Dr. Falk Pharma GmbH, Durect Corporation, Enanta Pharmaceuticals, Inc., ENYO Pharma SAS, Fast Forward Pharmaceuticals BV, Galectin Therapeutics Inc., Galmed Pharmaceuticals Ltd., Genfit SA, Gilead Sciences, Inc., GlaxoSmithKline plc, Immuron Limited, Ionis Pharmaceuticals, Inc., Islet Sciences, Inc., Madrigal Pharmaceuticals, Inc., MediciNova, Inc., Metacrine, Inc., MiNA Therapeutics, NGM Biopharmaceuticals, Inc., Novartis AG, Novo Nordisk A/S, NuSirt Biopharma, Inc., Shire plc, Viking Therapeutics, Inc. and Zydus Pharmaceuticals (USA) Inc. Ocaliva competes with UDCA (or ursodiol), a first-line therapy approved for the treatment of PBC that is available generically at a significantly lower cost than Ocaliva. Bezafibrate, a fibrate that is not approved by the FDA for any indication and is only available outside of the United States, has been studied in multiple clinical trials for the treatment of liver diseases including PBC and NASH. Genfit SA has an ongoing Phase 3 clinical trial of elafibranor, a dual PPAR alpha/delta agonist, in NASH. Genfit is also studying elafibranor for the treatment of PBC. Gilead Sciences, Inc. is conducting a Phase 3 clinical trial of selonsertib, an ASK-1 inhibitor, in NASH patients. Gilead Sciences, Inc. is also exploring additional studies in NASH for GS-0976, a small molecule allosteric inhibitor that acts at the protein-protein homodimer interface of acetyl-CoA carboxylases acquired from Nimbus Therapeutics, LLC, and an FXR agonist known as GS-9674. Gilead Sciences, Inc. is also studying a number of compounds in other liver diseases including PBC. Allergan plc has an ongoing Phase 3 clinical trial of cenicriviroc, a dual CCR2 and CCR5 inhibitor, for the treatment of NASH. A number of other companies have trials in PBC, NASH and other liver diseases we are targeting.

In addition, many universities and private and public research institutions may become active in our target disease areas. The results from our clinical trials and the approval of Ocaliva for PBC have brought more attention to our targeted indications and bile acid chemistry. As a result, we believe that additional companies and organizations may seek to compete with us in the future. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis, technologies and drug products that are more effective or less costly than OCA or any other product candidates that we are currently developing or that we may develop, which could render our products or product candidates obsolete and noncompetitive. Our ability to compete may also be affected because, in many cases, insurers or other third-party payors seek to encourage the use of generic products.

Off-label uses of other potential treatments may limit the commercial potential of our products and product candidates, especially given the pricing of Ocaliva and the anticipated pricing for our product candidates. For example, while fibrates are not approved for use in PBC, off-label use of fibrate drugs has been reported. In NASH, a number of treatments, including vitamin E (an antioxidant), insulin sensitizers (e.g., metformin, pioglitazone), antihyperlipidemic agents (e.g., gemfibrozil), pentoxifylline and UDCA, are used off-label. Although none of these treatments have been clearly shown in clinical trials to alter the course of the disease, in a previous study conducted by the NASH Clinical Research Network, improvements in certain histological measures of NASH were reported with vitamin E and pioglitazone. Various other treatments, both approved and unapproved, have been used in the other indications we are targeting.

We believe that our ability to successfully compete will depend on, among other things:

- the results of our and our strategic collaborators' clinical trials and preclinical studies;
- our ability to recruit and enroll patients for our clinical trials;
- the efficacy, safety and tolerability of Ocaliva and our other future approved products, if any;
- the speed at which we develop our product candidates;

- our ability to design and successfully execute appropriate clinical trials;
- our ability to maintain productive relationships with regulatory authorities;
- the timing and scope of regulatory approvals, if any;
- our ability to commercialize and market Ocaliva and our other future approved products, if any;
- the price of our products;
- our ability to obtain adequate levels of reimbursement under private and governmental health insurance plans, including Medicare;
- our ability to protect our intellectual property rights related to our products;
- our ability to manufacture and sell commercial quantities of Ocaliva and our other future approved products, if any, to the market; and
- the acceptance of our products by physicians and other healthcare providers.

If our competitors market products that are more effective or safe or less expensive than our products or that reach the market sooner than our products, we may not achieve commercial success. In addition, the biopharmaceutical industry is characterized by rapid technological change. Because our research approach integrates many technologies, it may be difficult for us to stay abreast of the rapid changes in other technologies. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Technological advances or products developed by our competitors may render our technologies, products or product candidates obsolete, less competitive or not economical.

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

We have formed a number of subsidiaries in jurisdictions outside of the United States in connection with or in anticipation of our commercial or other business activities in those jurisdictions. We are commercializing Ocaliva for PBC using a combination of our internal commercial organization, a contract sales organization and third-party distributors depending on the jurisdiction. In addition, Sumitomo Dainippon has an exclusive license to develop and commercialize OCA for the treatment of PBC and NASH in China (excluding Taiwan). Our international operations and business relationships subject us to additional risks that may materially adversely affect our business and ability to attain or sustain profitability, including:

- the far-reaching anti-bribery and anti-corruption legislation in the United Kingdom, including the UK Bribery Act, and elsewhere and escalation of investigations and prosecutions pursuant to such laws;
- compliance with complex import and export control laws;
- restrictions on direct investments by foreign entities and trade restrictions;
- differing regulatory requirements for drug approvals internationally and the inability to obtain necessary foreign regulatory, pricing or reimbursement approvals for our products in a timely manner, or at all;
- uncertainty regarding the collectability of accounts receivable;
- difficulties in staffing and managing international operations;
- potentially reduced protection for our intellectual property rights;
- potential third-party patent rights in countries outside of the United States;
- the potential for so-called ‘‘parallel importing,’’ which is what occurs when a local seller opts to import goods from another jurisdiction with relatively low prices, rather than buying them locally;
- unexpected changes in tariffs, trade barriers and regulatory requirements and the imposition of governmental controls;

- economic weakness, including inflation, or political instability, particularly in non-U.S. economies and markets, including countries in Europe;
- compliance with tax, employment, immigration and labor laws applicable to our employees working or traveling abroad;
- taxes in other countries;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other transactional risks incident to doing business in foreign countries;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from events affecting raw material supply or manufacturing capabilities abroad;
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters, including earthquakes, volcanoes, typhoons, floods, hurricanes and fires; and
- increasingly complex standards for complying with foreign laws and regulations that may differ substantially from country to country and may conflict with corresponding U.S. laws and regulations.

In June 2016, eligible members of the electorate in the United Kingdom decided by referendum to leave the European Union, in what is often referred to as Brexit. Negotiations for Brexit have caused political and economic uncertainty, including in the regulatory framework applicable to the operations of biotechnology and pharmaceutical companies, and this uncertainty may persist for years. Brexit could, among other outcomes, disrupt the free movement of goods, services and people between the United Kingdom and the European Union, result in changes to, and uncertainty regarding the application and interpretation of, national and international laws and regulations and introduce other legal and regulatory complexities. For example, because a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, Brexit could materially change the regulatory regime applicable to our operations, including with respect to Ocaliva for PBC and, if approved, OCA for NASH and our other product candidates. Such outcomes could make it more difficult and expensive for us to do business in Europe, complicate our clinical, manufacturing and regulatory strategies and impair our ability to obtain and maintain regulatory approval for, and, if approved, commercialize, our products and product candidates in Europe. In addition, our ability to continue to conduct our international operations out of the United Kingdom, where the headquarters for our international operations is located, may be materially and adversely affected. While we have undertaken a number of Brexit-related contingency planning initiatives, the full potential financial, legal, regulatory and other implications of Brexit are uncertain and we cannot make any assurances regarding the extent to which our business may be adversely affected thereby.

In addition, we are subject to the anti-bribery and anticorruption laws of the United States, as well as of foreign jurisdictions where we operate, including the U.S. Foreign Corrupt Practices Act and the UK Bribery Act. Generally, these laws prohibit paying or offering anything of value to a foreign government official for the purpose of obtaining or retaining business. U.S. and foreign regulators have increased their enforcement of anti-bribery and anticorruption laws in recent years, and failure to comply with these laws could result in various adverse consequences, including:

- the possible delay in approval or refusal to approve our product candidates;
- recalls, seizures or withdrawal from the market of an approved product;
- disruption in the supply or availability of our products or suspension of export or import privileges;
- the imposition of civil or criminal sanctions;
- the prosecution of executives overseeing our international operations; and
- damage to our reputation.

Any significant impairment of our ability to develop our product candidates or sell our approved products outside of the United States could adversely impact our business and financial results.

Our business and operations would suffer in the event of system failures, data breaches or violations of data protection laws.

We are increasingly dependent on information technology systems and infrastructure, including mobile technologies, to operate our business. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personally identifiable information. It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. The size and complexity of our information technology systems, and those of third-party vendors with whom we contract, and the volume of data we retain, make such systems potentially vulnerable to breakdown, malicious intrusion, security breaches and other cyber-attacks. Information security risks have significantly increased in recent years in part due to the proliferation of new technologies and the increased sophistication and activities of organized crime, hackers, terrorists and other external parties, including foreign state actors. A security breach or privacy violation that leads to disclosure or modification of, or prevents access to, personally identifiable information or other protected information could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to liability under laws and regulations that protect personal information, resulting in increased costs or loss of revenue. Similarly, the loss of clinical trial data from completed or ongoing or planned clinical trials could prevent us from obtaining regulatory approval or delay our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. If we are unable to prevent such security breaches or privacy violations or implement satisfactory remedial measures, our operations could be disrupted, and we may suffer loss of reputation, financial loss and other regulatory penalties because of lost or misappropriated information. In addition, these breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. Moreover, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information, trade secrets or other intellectual property. As cyber threats continue to evolve, we may be required to expend significant additional resources to continue to modify or enhance our protective measures or to investigate and remediate any information security vulnerabilities. While we have implemented security measures to protect our data security and information technology systems, such measures may not prevent such events. Significant disruptions of our information technology systems or breaches of data security could have a material adverse effect on our business, financial condition and results of operations.

Our information security systems are subject to laws and regulations requiring that we take measures to protect the privacy and security of certain information we gather and use in our business. For example, HIPAA, and its implementing regulations impose, among other requirements, certain regulatory and contractual requirements regarding the privacy and security of personal health information. In addition to HIPAA, numerous other federal and state laws, including, without limitation, state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use, disclosure and storage of personal information.

Various foreign countries where we may process personal information also have, or are developing, laws governing the collection, use, disclosure and storage of personal information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues that may affect our business. In July 2016, U.S. and European Commission officials adopted a new framework called the EU-U.S. Privacy Shield to govern cross-border flows of personal information. We adopted the EU-U.S. Privacy Shield and have certified to its requirements since October 2016.

In May 2018, the General Data Protection Regulation (the ‘‘GDPR’’) took effect in the European Union. The GDPR imposes more stringent data protection requirements, and provides for greater penalties for noncompliance, than previous EU data protection legislation. Although the GDPR applies across the European Union without the need for local implementing legislation, local data protection authorities retain the ability to interpret the GDPR, which has the potential to create inconsistencies on a country-by-country basis. In

addition, we do not know the extent of the impact that Brexit will have on our ability to transfer personal information between EU member states and the United Kingdom and we may need to develop new mechanisms to permit for the transfer of this data. Implementation of the GDPR and other changes in privacy and data protection laws or regulations could require changes to certain of our business practices, thereby increasing our costs. While we are actively employing the EU-U.S. Privacy Shield and the Swiss-U.S. Privacy Shield as a means to legitimize the transfer of personal information from the European Union and Switzerland to the United States, and are engaging in activities to comply with the GDPR requirements, we may be unsuccessful in these efforts.

The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues that may affect our business. There is a degree of uncertainty associated with the legal and regulatory environment around privacy and data protection laws, which continue to develop in ways we cannot predict, including with respect to evolving technologies, such as cloud computing. Privacy and data protection laws may be interpreted and applied inconsistently from country to country and impose inconsistent or conflicting requirements. Varying jurisdictional requirements could increase the costs and complexity of compliance or require us to change our business practices in a manner adverse to our business. A determination that we have violated privacy or data protection laws could result in significant damage awards, fines and other penalties that could, individually or in the aggregate, materially harm our business and reputation.

We have significantly expanded our operations and plan to continue our expansion to support our future development strategy for OCA for indications other than PBC, including NASH. We may experience difficulties in managing our significant growth.

We have significantly expanded our operations, including the size of our employee base, and expect to continue to grow as we pursue our future development and commercialization strategy. As we advance our preclinical and clinical development programs for OCA and our other product candidates, seek regulatory approval in the United States and elsewhere and increase the number of ongoing product development programs, we may need to increase our product development, scientific and administrative headcount. We will also need to grow our commercial capabilities. Such an evolution may impact our strategic focus and our deployment and allocation of resources. Our management, personnel and systems may experience difficulty in adjusting to our growth and strategic focus.

In addition, in order to continue to meet our obligations as a public company and to support our anticipated longer-term growth, we will need to increase our general and administrative capabilities. We have also expanded our operations geographically and formed a number of subsidiaries outside of the United States. In addition to our U.S. offices, we have an office in London, which serves as the headquarters for our international operations, and regional offices in a number of other countries, and we may further expand our geographical footprint. Our management, personnel and systems may not be adequate to support this future growth. Furthermore, we may face a number of complexities, such as being subject to national collective bargaining agreements for employees, in some of the countries in which we operate.

Our need to effectively manage our operations, growth and various projects requires that we:

- successfully attract and recruit new employees or consultants with the expertise and experience we require in the United States, Europe and other jurisdictions;
- manage our clinical programs effectively, which are often conducted at numerous domestic and international clinical sites, and advance our other development efforts;
- develop and expand our marketing and sales infrastructure; and
- continue to improve our operational, financial and management controls, reporting systems and procedures.

If we are unable to successfully manage our growth and the increased complexity of our operations, our business may be materially adversely affected.

We may not be able to manage our business effectively if we are unable to attract and retain key personnel and consultants.

We may not be able to attract or retain qualified personnel and consultants due to the intense competition for such individuals among biotechnology, pharmaceutical and other businesses. If we are not able to attract and retain necessary personnel and consultants to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development and commercial objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of Dr. Mark Pruzanski, our co-founder, president and chief executive officer, and the other members of our executive team, as well as other key employees and consultants. If we lose one or more of our executive officers or other key employees or consultants, our ability to implement our business strategy successfully could be seriously harmed. Any of our executive officers or other key employees or consultants may terminate their employment at any time and replacing such individuals may be difficult and time-consuming because of the limited number of individuals in our industry with the necessary breadth of skills and experience. Competition to hire and retain employees and consultants from this limited pool is intense, and we may be unable to hire, train, retain or motivate such individuals.

We also have key scientific and clinical advisors and consultants who assist us in formulating our research, development and clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us and such individuals typically will not enter into non-compete agreements with us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. In addition, our advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours.

Failure to establish and maintain adequate finance infrastructure and accounting systems and controls could impair our ability to comply with the financial reporting and internal controls requirements for publicly traded companies.

As a public company, we operate in a demanding regulatory environment, which requires us to comply with the Sarbanes-Oxley Act of 2002 and related rules and regulations, expanded disclosure requirements, accelerated reporting requirements and complex accounting rules. Responsibilities imposed by the Sarbanes-Oxley Act include establishing and maintaining corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud.

In particular, our compliance with Section 404 of the Sarbanes-Oxley Act has required and will continue to require that we incur substantial accounting-related expenses and expend significant management efforts. Our testing, or the testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls that we would be required to remediate in a timely manner. If we are not able to comply with the requirements of the Sarbanes-Oxley Act, we could be subject to sanctions or investigations by the SEC, the Nasdaq Stock Market or other regulatory authorities, which would require additional financial and management resources and could adversely affect the market price of our securities. Furthermore, if we cannot provide reliable financial reports or prevent fraud, our business and results of operations would likely be materially adversely affected.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading, which could significantly harm our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with the regulations of the FDA, the SEC or other domestic or foreign regulators, provide accurate information to the FDA, the SEC or other domestic or foreign regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive regulation in the United States and

abroad intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. Such laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. Misconduct and misappropriation of confidential information by our employees or third parties may also include improper trading in our securities, which may harm our reputation and result in enforcement actions against us. We have adopted a global code of business conduct and implemented a corporate compliance program, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental inquires, investigations or other actions or lawsuits stemming from a failure to comply with applicable laws or regulations. The outcome of any such inquiry, investigation, action or lawsuit could have a significant negative impact on our business, including as a result of the imposition of significant fines or other sanctions. In addition, the institution of any such inquiry, investigation, action or lawsuit could negatively impact the market price of our securities.

We face potential product liability exposure, and if successful claims are brought against us, we may incur substantial liability for our products or product candidates and may have to limit or suspend their use.

The use of our product candidates in clinical trials and the sale of any products for which we may obtain marketing approval, such as Ocaliva for PBC, expose us to the risk of product liability claims. Product liability claims may be brought against us or our collaborators by participants enrolled in our clinical trials, patients, healthcare providers or others. If we cannot successfully defend ourselves against any such claims, we may incur substantial liabilities. Regardless of their merit or eventual outcome, product liability claims may result in:

- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire clinical trial programs;
- costs of related litigation;
- substantial monetary awards to patients or other claimants;
- decreased demand for our products and loss of revenues;
- impairment of our business reputation;
- diversion of management and scientific resources from our business operations; and
- the inability to develop and commercialize our products and product candidates or the withdrawal of our products from the market.

We have obtained limited product liability insurance coverage. Our insurance coverage may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to product liability. Large judgments have been awarded in class action lawsuits based on the unanticipated side effects of drug products. A successful product liability claim or series of claims brought against us, particularly if judgments exceed our insurance coverage, could decrease our cash resources and adversely affect our business.

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

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, employment practices liability, property, auto, workers' compensation, products liability and directors' and officers' insurance. We do not know, however, if our current levels of coverage are adequate or if we will be able to obtain insurance with adequate levels of coverage in the future, if at all. Any significant uninsured liability may require us to pay substantial amounts, which could materially adversely affect our financial position and results of operations. Furthermore, any

increase in the volatility of our stock price, among other factors, may result in us being required to pay substantially higher premiums for our directors' and officers' insurance, and may make it difficult for us to obtain adequate coverage on reasonable terms, if at all.

If we engage in an in-license transaction, acquisition, reorganization or business combination, we will face a variety of risks that could adversely affect our business operations and our securityholders.

From time to time, we have considered, and we will continue to consider in the future, strategic business initiatives intended to further the expansion and development of our business. These initiatives may include in-licensing or acquiring products, technologies or businesses or entering into a business combination with another company. If we pursue such a strategy, we could, among other things:

- issue equity securities that would dilute our current stockholders' ownership;
- incur substantial debt that may place strains on our operations;
- be required to dedicate substantial operational, financial and management resources to integrate new products, technologies or businesses;
- assume substantial actual or contingent liabilities;
- impair our ability to make payments of interest and principal on our outstanding debt, including the Convertible Notes;
- reprioritize our development programs or cease development and commercialization activities with respect to certain of our product candidates or approved products; or
- merge or otherwise enter into a business combination with another company, which may result in our stockholders receiving cash and/or shares of the other company on terms that certain of our stockholders may not deem desirable.

We may use our limited financial and human resources to pursue a particular research program or product candidate that is ultimately unsuccessful or less successful than other programs or product candidates that we may have forgone or delayed.

Because we have limited resources, we may forego or delay the development of certain programs or product candidates that later prove to have greater commercial potential than the programs or product candidates that we do pursue. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for product candidates may not yield any commercially viable products. If we fail to accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other arrangements or we may allocate our limited internal resources to that product candidate when it would have been more advantageous to enter into such an arrangement. Any such failure could have a material adverse effect on our business, financial condition or results of operations.

Changes in our effective income tax rate could adversely affect our results of operations.

We are subject to income taxes in the United States and various foreign jurisdictions. Various factors may have favorable or unfavorable effects on our effective income tax rate. These factors include, but are not limited to, interpretations of existing tax laws, changes in tax laws and rates, the accounting for stock options and other stock-based compensation, changes in accounting standards, future levels of research and development spending, changes in the mix and level of pre-tax earnings in different jurisdictions, the outcome of audits or other examinations by the U.S. Internal Revenue Service and tax regulators in other jurisdictions, the accuracy of our estimates for unrecognized tax benefits, the realization of deferred tax assets and changes to our ownership or capital structure.

In late 2017, the United States enacted the Tax Cuts and Jobs Act of 2017 (the ''TCJA''), which significantly changed U.S. tax law, including by implementing a reduction in the corporate tax rate to 21%, moving from a worldwide tax system to a territorial system and imposing new or additional limitations on the deductibility of interest expense and executive compensation.

The impact on our effective income tax rate resulting from the above-mentioned factors and others may be significant and could adversely affect our results of operations.

Risks Related to Our Intellectual Property

It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection. If our patent position does not adequately protect our products such as Ocaliva and product candidates, others may compete against us more directly, which could harm our business, possibly materially.

Our commercial success will depend in part on our ability to obtain and maintain patent, trademark and trade secret protection covering our products such as Ocaliva and product candidates, as well as our ability to successfully defend our intellectual property against third-party challenges. Our ability to stop third parties from making, using, selling, offering to sell or importing our products is dependent upon the extent to which we have regulatory exclusivity or intellectual property-based exclusivity rights under valid and enforceable patents or other intellectual property that cover our products. If we fail to obtain and maintain adequate intellectual property protection, we may not be able to prevent third parties from launching generic versions of our products, from using our proprietary technologies or from marketing products that are very similar or identical to ours.

The patent positions of 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 foreign jurisdictions, and the legal standards relating to the patentability, validity and enforceability of pharmaceutical patents are evolving. Changes in either the patent laws or in interpretations of patent laws in U.S. and foreign jurisdictions may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be enforced in the patents that we currently own or that may issue from the applications we have filed or may file in the future or those that we may license from third parties. Additionally, our currently pending or future patent applications may not result in issued patents, and any term extensions that we seek may not be granted. Further, if any patents we obtain or license are deemed invalid or unenforceable, it could impact our ability to commercialize or license our technology or we may not be able to prevent third parties from launching generic versions of our products, or from developing or marketing products that are similar or identical to ours.

There have been numerous changes to the patent laws that may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. In September 2011, the America Invents Act was signed into law. The final substantive provisions of the America Invents Act became effective in March 2013. The America Invents Act included a number of significant changes to U.S. patent law that affect the way patent applications are filed, prosecuted and litigated, including, among other things, changing from a ‘‘first to invent’’ to a ‘‘first inventor to file’’ system and creating processes, such as Inter Partes Review (‘‘IPR’’) and other post-grant review processes, that permit third parties to challenge the patentability of granted patents before the Patent Trial and Appeal Board of the U.S. Patent and Trademark Office (the ‘‘USPTO’’). The IPR process, for example, permits any person to challenge the validity of a patent on the grounds that it was anticipated or made obvious by prior art. 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, financial condition, results of operations and growth prospects.

Others have filed, and in the future, are likely to file, patent applications covering products and technologies that are similar or competitive to ours, or may be 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 infringement, interference, derivation, opposition, nullity, invalidity or other similar proceedings before U.S. or non-U.S. patent offices.

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. For example:

- others may be able to make compounds that are similar to our products or 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 patents or 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 may duplicate any of our technologies;
- any patents that we obtain may not provide us with any competitive advantages or exclusivity in a particular product area or indication or for the length of time we have anticipated;
- we may not develop additional proprietary technologies that are patentable; or
- the patents of others may have an adverse effect on our business.

We are the owner of record of numerous issued U.S. and non-U.S. patents with claims directed to pharmaceutical compounds, pharmaceutical compositions, methods of making these compounds and methods of using these compounds in various indications. In addition, we are the owner of record of numerous pending U.S. and non-U.S. patent applications, and regularly pursue additional patent applications in various jurisdictions.

The issued composition of matter patents for OCA are expected to expire in 2022 at the earliest and 2036 at the latest if the appropriate maintenance, renewal, annuity, or other government fees are paid. Without patent protection, including patent protection covering the composition of matter of our products and product candidates, our ability to stop others from using or selling our products and product candidates may be limited.

Due to the patent laws of a country, the decisions of a patent examiner in a country or our own filing strategies, we may not obtain patent coverage for all of our products and product candidates or methods involving these candidates in the parent patent application. While we plan to pursue divisional patent applications or continuation patent applications in the United States and other countries to obtain claim coverage for inventions which were disclosed but not claimed in the parent patent application, we cannot be certain that such patents will be granted or that the scope of any patent granted will prevent third parties from selling the same or similar products.

If we do not obtain protection under the Hatch-Waxman Act and similar legislation outside of the United States by extending the patent terms and obtaining data exclusivity for our products and product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our products, U.S. patents may be eligible for a limited extension of patent term under the Hatch-Waxman Act. The Hatch-Waxman Act permits an extension of patent term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, an extension may not be granted because of, for example, failure to apply within applicable deadlines, failure to apply prior to expiration of relevant patents or failure to satisfy applicable requirements. Moreover, the applicable time period or scope of patent protection afforded could be less than what is requested. 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, our competitors may obtain approval of competing products following our patent expiration and our revenue could be reduced, possibly materially.

Our primary composition of matter patent for OCA expires in 2022. In light of the U.S. marketing approval of Ocaliva for PBC in May 2016, we have applied for an extension of the patent term for this patent in the United States through 2027. In addition, in connection with the conditional approval of Ocaliva for PBC in the European Union, we have applied for SPC to extend the patent term for this patent in the European Union through 2027. We have received grants of SPC in Austria, Denmark, France, Germany, Ireland, Italy, Norway, Spain and Sweden and we expect to take similar actions in other jurisdictions and

countries where similar regulations exist. The issued composition of matter patents for OCA are expected to expire in 2022 at the earliest and 2036 at the latest if the appropriate maintenance, renewal, annuity, or other government fees are paid.

We may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights, and such litigation may divert the attention of our management and scientific personnel and adversely affect our development and commercialization efforts.

If we choose to go to court or engage in other adversarial proceedings to stop another party from using the inventions claimed in any patents we obtain, that individual or company has the right to ask the court or adjudicating body to rule that such patents are invalid, not infringed or should not be enforced against that third party. These lawsuits and proceedings are expensive and would consume time and resources and divert the attention of management and scientific personnel even if we are successful in defending our rights. In addition, there is a risk that such court or adjudicating body will decide that such patents are invalid, unenforceable or not infringed, and that we do not have the right to stop the other party from using the inventions. In addition, the U.S. Supreme Court has modified some tests used by the USPTO in granting patents over the past 20 years, which may decrease the likelihood that we will be able to obtain patents and increase the likelihood of challenge of any patents we obtain or license.

We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing our products and product candidates.

Our success will depend in part on our ability to operate without infringing the proprietary rights of third parties. We cannot guarantee that our products, or the manufacture or use of our product candidates, will not infringe third-party patents. Furthermore, a third party may claim that we or our manufacturing or commercialization partners are using inventions covered by the third party's patent rights and may go to court to stop us from engaging in our normal operations and activities, including making or selling our products and product candidates. These lawsuits are costly and could affect our results of operations and divert the attention of management and scientific personnel. There is also a risk that a court would decide that we or our manufacturing or commercialization partners are infringing the third party's patents and would order us or our partners to stop the activities covered by the patents. In that event, we or our partners may not have a viable way around the patent and may need to halt commercialization or development of the relevant product or product candidate. In addition, there is a risk that a court will order us or our partners to pay the other party damages for having violated the other party's patents, and we may be subject to indemnification obligations with respect to any such payments made by our partners. 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, product candidates or methods of use. The coverage of patents is subject to interpretation by the courts, and such interpretation is not always uniform.

If we are sued for patent infringement, we would need to demonstrate that our products, product candidates 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 this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in such proceedings, we may incur substantial costs and divert management's time and attention, which could have a material adverse effect on our business. 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 fail to obtain a license, develop or obtain non-infringing technology, defend an infringement action successfully or have infringed patents declared invalid, we may incur substantial monetary damages, encounter significant delays in bringing our products and product candidates to market and be precluded from manufacturing or selling our products and product candidates.

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 or file with respect to a technology, because:

- some patent applications in the United States may be unpublished or otherwise maintained in secrecy until the patents are issued;
- 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.

Our competitors may have filed, and may in the future file, patent applications covering technology similar to ours. 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, derivation or other similar 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, 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 such patent applications 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 financial and other resources. In addition, uncertainties resulting from the initiation and continuation of any such litigation could have a material adverse effect on the market price of our securities and our ability to raise the funds necessary to continue our operations.

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 as a result of non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on our patents and patent applications are required to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of such patents and patent applications. In addition, the USPTO and foreign patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We have implemented systems and engaged reputable third-party service providers to help ensure that we comply with such requirements on a timely basis, but inadvertent lapses may occur and there are situations in which noncompliance can result in abandonment or lapse of the relevant patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Any such event may impair our competitive position in the relevant jurisdiction and have a material adverse effect on our financial condition or results of operations.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers. If we are not able to adequately prevent disclosure of trade secrets and other proprietary information, the value of our technology, products and product candidates could be significantly diminished.

As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees, or we, have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims, which could result in substantial costs and be a distraction to management even if we are successful.

We may 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, and may not prevent others from independently and lawfully developing similar or identical products that circumvent our intellectual property. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to protect our trade secrets and other proprietary information. 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.

Third parties, including competitors of ours, may also independently discover our trade secrets or other proprietary information. In addition, we may be required under U.S. or foreign transparency initiatives or other regulations to publicly disclose or otherwise make available certain information that we consider to be proprietary, including pre-clinical and clinical research data. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets or other proprietary information is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside of the United States are sometimes reluctant to protect trade secrets. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain protection of our trade secrets and other proprietary information could adversely affect our competitive business position.

We have not yet registered all of our trademarks and failure to secure such registrations could adversely affect our business.

We have numerous trademark and service mark registrations and pending trademark and service mark applications in the United States and abroad.

Our trademark applications may not be allowed for registration and our registered trademarks may not be maintained or enforced. During prosecution of applications for trademark registration, we may receive rejections or refusals. Although we are given an opportunity to respond, we may be unable to overcome such rejections. In addition, the USPTO and comparable agencies in many other jurisdictions provide third parties with an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings have been filed and may in the future be filed against certain of our trademarks, and our trademarks may not survive such proceedings. If we do not secure registrations for our trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would.

Trademark protection varies in accordance with local laws. Trademarks remain in force in some countries as long as the trademark is used and in other countries as long as the trademark is registered. Trademark registrations generally are for fixed but renewable terms. We cannot provide any assurances that any trademarks or service marks will be sufficient to prevent competitors from adopting similar names. The adoption of similar names by competitors could impede our ability to build brand identity and may lead to customer confusion, which could adversely affect our sales or profitability.

Risks Related to Our Indebtedness

Servicing our debt will require significant amounts of cash, and we may not have sufficient cash flow from our business to pay our debt.

Our ability to make scheduled payments of the principal of, to pay interest on or to refinance the $460.0 million aggregate principal amount of Convertible Notes that we issued in July 2016 or any other indebtedness we or our subsidiaries may incur in the future depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may not generate cash flow from operations in the future sufficient to service our debt, including the Convertible Notes. If we are unable to generate cash flow, we may be required to adopt one or more alternatives, such as selling assets, restructuring debt or obtaining additional equity capital on terms that may be unfavorable to us or highly dilutive. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at the time we seek to refinance such indebtedness. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

We may incur substantially more debt or take other actions that would affect our ability to pay the principal of and interest on our debt.

We and our subsidiaries may be able to incur substantial additional debt in the future, some of which may be secured debt. We and our subsidiaries are not restricted under the terms of the indenture governing the Convertible Notes or otherwise from incurring additional debt, securing existing or future debt, recapitalizing our debt or taking other actions that could have the effect of diminishing our ability to service our debt when due.

The accounting method for convertible debt securities that may be settled in cash, such as the Convertible Notes, could have a material effect on our reported financial results.

Under Accounting Standards Codification Subtopic 470-20, ''Debt with Conversion and Other Options'' (''ASC 470-20''), an entity must separately account for the liability and equity components of convertible debt instruments (such as the Convertible Notes) that may be settled entirely or partially in cash upon conversion in a manner that reflects the issuer's economic interest cost. The effect of ASC 470-20 on the accounting for the Convertible Notes is that the equity component is required to be included in the additional paid-in capital section of stockholders' equity on our consolidated balance sheet, and the value of the equity component is treated as original issue discount for purposes of accounting for the debt component of the Convertible Notes. As a result, we are required to record a greater amount of non-cash interest expense in current periods presented as a result of the amortization of the discounted carrying value of the Convertible Notes to their face amount over the term of the Convertible Notes. Because ASC 470-20 requires interest to include both the current period's amortization of the debt discount and the instrument's coupon interest, we report lower net income in our financial results, which could adversely affect the market price of our common stock and the market price of the Convertible Notes.

In addition, under certain circumstances, convertible debt instruments (such as the Convertible Notes) that may be settled entirely or partly in cash are currently accounted for utilizing the treasury stock method, the effect of which is that the shares issuable upon conversion of the Convertible Notes will not be included in the calculation of diluted earnings per share except to the extent that the conversion value of the notes exceeds their principal amount. Under the treasury stock method, for diluted earnings per share purposes, the transaction is accounted for as if the number of shares of common stock that would be necessary to settle such excess, if we elected to settle such excess in shares, are issued. We cannot be sure that the accounting standards in the future will continue to permit the use of the treasury stock method. If we are unable to use the treasury stock method in accounting for the shares issuable upon conversion of the Convertible Notes, then our diluted earnings per share would be adversely affected.

Risks Related to Ownership of Our Common Stock

Ownership in our common stock is highly concentrated and your ability to influence corporate matters may be limited as a result.

Our executive officers, directors and stockholders who own more than 5% of our outstanding common stock together beneficially own a significant percentage of our common stock based on reports filed with the SEC. If these stockholders were to choose to act together, they would be able to significantly influence matters submitted to our stockholders for approval, including the election of directors and approval of any merger, consolidation, sale of all or substantially all of our assets or other business combination or reorganization, as well as our management and affairs. This concentration of voting power could delay or prevent an acquisition of us on terms that other stockholders may desire. The interests of this group of stockholders may not always coincide with your interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the market price of our common stock.

We have a significant stockholder, which will limit your ability to influence corporate matters, may give rise to conflicts of interest and could result in future substantial sales of shares of our common stock into the market.

Genextra S.p.A. (''Genextra'') is our largest stockholder and owns a significant minority percentage of our outstanding common stock. Accordingly, Genextra exerts and will continue to exert significant influence over us and any action requiring the approval of the holders of our common stock, including the election of directors and amendments to our organizational documents, such as increases in our authorized shares of common stock and approval of significant corporate transactions. This concentration of voting power makes it less likely that any other holder of common stock will be able to affect the way we are managed and could delay or prevent an acquisition of us on terms that other stockholders may desire.

Furthermore, the interests of Genextra may not always coincide with your interests or the interests of other stockholders, and Genextra may act in a manner that advances its best interests and not necessarily those

of other stockholders, including seeking a premium value for its common stock, and might affect the market price of our common stock. Our board of directors, which consists of ten directors, including one associated with Genextra, has the power to set the number of directors on our board from time to time.

Genextra also may sell shares of our common stock into the market from time to time, and we cannot predict the effect, if any, that future sales by Genextra may have on the market price of our common stock. In addition, Genextra has informed us that it has pledged shares of our common stock that it holds as collateral in connection with a margin loan. Enforcement against such collateral could materially and adversely affect the price of our common stock.

An active trading market in our common stock may not be maintained.

The trading market in our common stock has been extremely volatile. The quotation of our common stock on the Nasdaq Global Select Market does not assure that a meaningful, consistent and liquid trading market will exist. We cannot predict whether an active market for our common stock will be maintained in the future. An absence of an active trading market could adversely affect your ability to sell our common stock at current market prices in short time periods, or possibly at all. Additionally, market visibility for our common stock may be limited and such lack of visibility may have a depressive effect on the market price for our common stock.

We have previously been, and are currently, subject to securities class action litigation and may be subject to similar or other litigation in the future. Such matters can be expensive, time-consuming and have a material adverse effect on our business, results of operations and financial condition.

We have previously been subject to securities class action lawsuits. In February 2014, two purported securities class actions were filed against us and certain of our officers, which were eventually consolidated. In May 2016, the defendants reached an agreement with the lead plaintiff to seek court approval of a proposed resolution and the settlement was ultimately granted final approval by the court in September 2016. While the final judgment and order of the court included a dismissal of the action with prejudice against all defendants and the defendants did not admit any liability as part of the settlement, the total payment aggregated to $55.0 million, of which $10.0 million was paid by our insurers.

In September 2017, a lawsuit and, in January 2018, a follow-on lawsuit were filed alleging that we and certain of our officers made material misrepresentations and/or omissions of material fact regarding Ocaliva dosing, use and pharmacovigilance-related matters, as well as our operations, financial performance and prospects. The plaintiffs seek unspecified monetary damages on behalf of the putative class, an award of costs and expenses, including attorney's fees, and rescissory damages. While we believe that we have a number of valid defenses to the claims described above and intend to vigorously defend ourselves, the matters are in the early stages of litigation and no assessment can be made as to the likely outcome of the matters or whether they will be material to us.

We may be subject to additional suits or proceedings brought in the future and, as has been the case with many companies in our industry, we may from time to time receive inquiries and subpoenas and other types of information requests from government authorities and others. For example, in May 2018, we received a subpoena from the SEC requesting information in connection with our patient assistance program and certain of our commercial activities. While the ultimate outcome of any such investigations, inquiries, information requests and legal proceedings is difficult to predict, adverse resolutions or settlements of those matters may result in, among other things, modification of our business practices, product recalls, significant costs, payments, damages or fines or other administrative, civil or criminal remedies, liabilities or penalties, which may have a material adverse effect on our business, results of operations and financial condition. In addition, monitoring and defending against legal actions, whether or not meritorious, and responding to investigations, inquiries and information requests is expensive, time-consuming for our management and detracts from our ability to fully focus our internal resources on our business activities, and we cannot predict how long it may take to resolve such matters. Although we may receive insurance coverage for certain adversarial proceedings, coverage could be denied or prove to be insufficient. It is possible that we could, in the future, incur judgment or enter into settlement of claims for monetary damages. A decision adverse to our interests could result in the payment of substantial damages and could have a material adverse effect on our business, results of operations and financial condition.

Our stock price has been and may in the future be volatile, which could cause holders of our common stock to incur substantial losses.

The market price of our common stock has been, and is likely to continue to be, highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. Since our IPO in October 2012, the price of our common stock on the Nasdaq Global Select Market has ranged from $17.96 per share to $497.00 per share. In addition to the other factors discussed in this ''Risk Factors'' section and elsewhere in this Annual Report on Form 10-K, the factors that may result in wide fluctuations in the price of our common stock include any:

- failure to successfully commercialize Ocaliva for PBC in the United States, Europe, Canada, Israel, Australia and other jurisdictions in which we have or may receive marketing authorization or our inability to maintain regulatory approval for Ocaliva in such jurisdictions or receive marketing authorization for Ocaliva in other jurisdictions;
- issues, delays or failures in identifying patients, enrolling patients, treating patients, meeting specific endpoints in the jurisdictions in which we intend to seek approval or completing and timely reporting the results of our NASH or PBC clinical trials;
- inability to obtain additional funding;
- delay in filing an IND, NDA, MAA or comparable submission for any of our product candidates, including OCA for NASH, and any adverse development or perceived adverse development with respect to the regulatory review of any such submission;
- failure to successfully develop, obtain regulatory approval of and, if approved, commercialize OCA for indications other than PBC, such as NASH, or any of our other product candidates;
- potential side effects associated with Ocaliva for PBC, OCA for NASH or our other product candidates;
- inability to obtain adequate product supply of Ocaliva, OCA or any of our other product candidates or the inability to do so at acceptable prices;
- results of clinical trials of our competitors' products and product candidates;
- regulatory actions with respect to our products or product candidates or our competitors' products or product candidates;
- changes in laws or regulations applicable to our products or product candidates;
- failure to meet or exceed financial projections or guidance we may provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;
- actual or anticipated fluctuations in our financial condition and operating results;
- actual or anticipated changes in our growth rate relative to our competitors;
- actual or anticipated fluctuations in our competitors' operating results or changes in their growth rate;
- competition from existing products or new products that may emerge;
- announcements by us, our collaborators or our competitors of significant acquisitions, strategic collaborations, joint ventures, collaborations or capital commitments;
- issuance of new or updated research or reports by securities analysts;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- additions or departures of key management or scientific personnel;

- disputes or other developments related to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- announcement or expectation of additional financing efforts;
- disputes, governmental inquiries or investigations, legal proceedings or litigation, including any securities, intellectual property, employment, product liability or other litigation;
- sales of our common stock by us, our insiders or our other stockholders;
- failure to adopt appropriate information security systems, including any systems that may be required to support our growing and changing business requirements, or prevent system failures, data breaches or violations of data protection laws;
- market conditions for biopharmaceutical stocks in general; and
- general economic, industry and market conditions.

Furthermore, stock markets in general and the market for biotechnology companies in particular have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many companies. These fluctuations often have been unrelated or disproportionate to the operating performance of those companies. These broad market and industry fluctuations, as well as general economic, political and market conditions such as recessions, interest rate changes or international currency fluctuations may negatively impact the market price of shares of our common stock, regardless of our actual operating performance. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We have been in the past, and are currently subject to this type of litigation, which could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business. As a result of this volatility, you could incur substantial losses.

In addition, pursuant to the securities purchase agreement that we entered into with the purchasers in the Concurrent Private Placement, such purchasers have the right, subject to certain conditions, to require us to file a registration statement covering the sale of their shares of our common stock purchased in the Concurrent Private Placement. If such registration rights are exercised and we register the offer and sale of these shares, the shares may be freely sold in the public market.

If our stockholders sell substantial amounts of our common stock, the market price of our common stock may decline even if our business is doing well.

A significant number of shares of our common stock are held by a small number of stockholders, including Genextra. Sales of a significant number of shares of our common stock, or the expectation that such sales may occur, could significantly reduce the market price of our common stock. These sales, or the possibility that these sales may occur, also might make it more difficult for us to sell equity securities in the future at a time and price that we deem appropriate. We have also registered the offer and sale of all of the shares of common stock that we may issue under our equity compensation plans, including upon the exercise of stock options. These shares may be freely sold in the public market upon issuance.

Additionally, sales of our common stock by our executive officers or directors, even when done during an open trading window under our policies with respect to insider sales or done under a trading plan adopted in accordance with the guidelines set forth by Rule 10b5-1, may adversely impact the market price of our common stock. Although we do not expect that the relatively small volume of such sales would itself significantly impact the market price of our common stock, the market could react negatively to the announcement of such sales, which could in turn affect the market price of our common stock. Furthermore, Genextra has informed us that it has pledged shares of our common stock that it holds as collateral in connection with a margin loan. Enforcement against such collateral could materially and adversely affect the price of our common stock.

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

We are subject to the periodic reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file

or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosure due to error or fraud may occur and not be detected.

You may experience future dilution as a result of future equity offerings or strategic transactions.

We may raise additional funds through the issuance and sale of additional shares of our common stock or other securities convertible into or exchangeable for our common stock. For example, in April 2018, we issued and sold an aggregate of 4,257,813 shares of common stock and in July 2016, we issued and sold $460.0 million of Convertible Notes. Conversions of the Convertible Notes dilute the ownership interests of existing shareholders to the extent that we elect to deliver shares of our common stock (or a combination of cash and shares of our common stock) in connection therewith. In addition, the existence of the Convertible Notes may encourage short selling by market participants because the conversion of the Convertible Notes could depress the price of our common stock. We may also issue shares of common stock, stock options, restricted stock, restricted stock units or other stock-based awards under our existing or future equity incentive plans or other employee or director compensation plans. The issuance of additional shares of common stock (including pursuant to conversions of the Convertible Notes) or other securities convertible into or exchangeable for our common stock, or the perception that such issuances may occur, may materially and adversely affect the price of our common stock.

If securities or industry analysts cease publishing research or reports about us, our business or our market, or if they publish inaccurate or unfavorable reports about us or our common stock, the price of our common stock and its trading volume could decline.

The market for our common stock depends in part on the research and reports that securities or industry analysts publish about our company. We do not have any control over these analysts, and there can be no assurance that analysts will continue to cover us or provide favorable coverage. If one or more of the analysts who cover us downgrade our common stock or publish inaccurate or unfavorable research about our business, our stock price may decline. If one or more of the analysts covering us fail to regularly publish reports on us, demand for our common stock may decline, which could cause our stock price and trading volume to decline.

Anti-takeover provisions in our restated certificate of incorporation and our restated bylaws, as well as provisions of Delaware law and certain provisions of the Convertible Notes, might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the market price of our common stock.

Provisions in our restated certificate of incorporation and restated bylaws, as well as provisions of Delaware law, may discourage, delay or prevent a merger, acquisition or other change in control that our stockholders consider favorable, including transactions in which you might otherwise receive a premium for your shares of our common stock. These provisions may also prevent or frustrate attempts by our stockholders to replace or remove our management. Our corporate governance documents include provisions:

- authorizing the issuance of ‘‘blank check’’ convertible preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders, to the extent that no stockholder, together with its affiliates, holds more than 50% of our voting stock;
- eliminating the ability of stockholders to call a special meeting of stockholders;

- permitting our board of directors to accelerate the vesting of outstanding equity awards upon certain transactions that result in a change of control; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

In addition, as a Delaware corporation, we are subject to provisions of Delaware law, including Section 203 of the Delaware General Corporation Law (the ''DGCL''), which prevents some stockholders holding more than 15% of our outstanding common stock from engaging in certain business combinations without approval of the holders of substantially all of our outstanding common stock. Any provision of our restated certificate of incorporation or restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Certain provisions of the Convertible Notes could also make it more difficult or more expensive for a third party to acquire us. For example, if an acquisition event constitutes a ''fundamental change'' under the terms of the Convertible Notes, holders of the Convertible Notes will have the right to require us to purchase their Convertible Notes for cash. Similarly, if an acquisition event constitutes a ''make-whole fundamental change'' under the terms of the Convertible Notes, we may be required to increase the conversion rate for holders who convert their Convertible Notes in connection with such make-whole fundamental change.

The existence of the foregoing provisions and anti-takeover measures may also frustrate or prevent any attempts by our stockholders to replace or remove our current management or members of our board of directors and could limit the price that investors might be willing to pay in the future for shares of our common stock. They could also deter potential acquirers of our company, thereby reducing the likelihood that you could receive a premium for your common stock in an acquisition.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful stockholder claims against us and may reduce the amount of money available to us.

As permitted by Section 102(b)(7) of the DGCL, our restated certificate of incorporation limits the liability of our directors to the fullest extent permitted by law. In addition, as permitted by Section 145 of the DGCL, our restated certificate of incorporation and restated bylaws provide that we shall indemnify, to the fullest extent authorized by the DGCL, each person who is involved in any litigation or other proceeding because such person is or was a director or officer of our company, or is or was serving as an officer or director of another entity at our request, against all expense, loss or liability reasonably incurred or suffered in connection therewith. Our restated certificate of incorporation provides that the right to indemnification includes the right to be paid expenses incurred in defending any proceeding in advance of its final disposition, subject to certain conditions. The rights conferred in the restated certificate of incorporation and the restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.

The above limitations on liability and our indemnification obligations limit the personal liability of our directors and officers for monetary damages for breach of their fiduciary duty as directors by shifting the burden of such losses and expenses to us. Although we carry directors' and officers' liability insurance, certain liabilities or expenses covered by our indemnification obligations may not be covered by such insurance or the coverage limitation amounts may be exceeded. As a result, we may need to use a significant amount of our funds to satisfy our indemnification obligations, which could severely harm our business and financial condition and limit the funds available to stockholders who may choose to bring a claim against our company.

We do not intend to pay dividends in the foreseeable future.

We do not anticipate paying cash dividends in the future. As a result, only appreciation of the price of our common stock will provide a return to stockholders, which may not occur. Investors seeking cash dividends should not invest in our common stock. You may not realize any return on your investment in our common stock and may lose some or all of your investment.

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

We have significant net operating loss carryforwards (''NOLs'') for U.S. Federal income tax purposes. The enactment of the TCJA in late 2017 modified the ability of companies to utilize NOLs arising in tax years beginning on or after January 1, 2018 by providing that such NOLs may be carried-forward indefinitely and used to offset up to 80 percent of taxable income in any given future year. Existing NOLs that arose in tax years beginning prior to January 1, 2018 were not affected by the TCJA and are generally eligible to be carried-forward for up to 20 years and used to fully offset taxable income in future years. Our pre-2018 NOLs will expire for U.S. Federal income tax purposes between 2024 and 2037. We also have certain state and foreign NOLs in varying amounts depending on the different state and foreign tax laws.

In addition, our ability to utilize our NOLs may be limited under Section 382 of the Internal Revenue Code or similar rules. The Section 382 limitations apply if an ''ownership change'' occurs. Generally, an ownership change occurs when certain shareholders increase their aggregate ownership by more than 50 percentage points over their lowest ownership percentage in a testing period (typically three years). We have evaluated whether one or more ownership changes under Section 382 have occurred since our inception and have determined that there have been at least two such changes. Although we believe that these ownership changes have not resulted in material limitations on our ability to use these NOLs, our ability to utilize these NOLs may be limited due to future ownership changes or for other reasons. As a result, we may not be able to take full advantage of our carryforwards for U.S. federal, state, and foreign tax purposes.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our corporate headquarters are located at 10 Hudson Yards in New York, New York, where we lease and occupy an aggregate of approximately 41,100 square feet of office space. The lease covering this property is currently scheduled to expire at varying times through June 2021.

Our research and development operations are based in San Diego, California, where we lease and occupy an aggregate of approximately 47,000 square feet of space. The lease covering this property is currently scheduled to expire in July 2020.

We also lease and occupy approximately 8,500 square feet of office space in London, United Kingdom, which serves as the headquarters for our international operations. The lease covering this property is currently scheduled to expire in May 2024.

We believe that our existing facilities are adequate for our immediate needs and that, should it be needed, additional space can be leased to accommodate any future growth.

Item 3. Legal Proceedings

For a description of our significant legal proceedings, see Note 15 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K and incorporated by reference herein.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

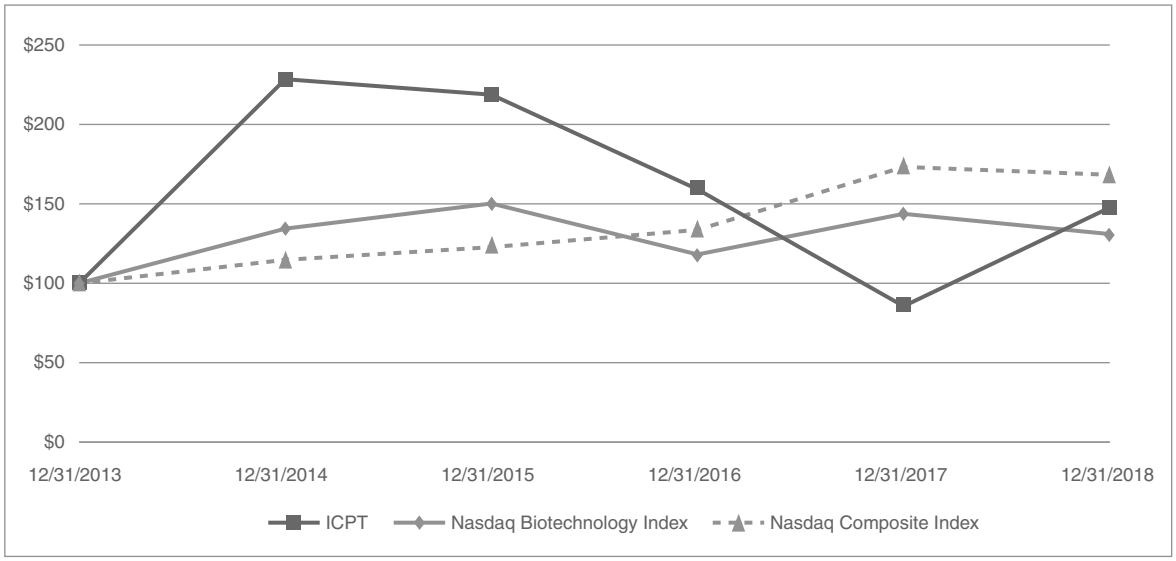
Market Information and Stockholders

Our common stock trades on the Nasdaq Global Select Market under the symbol ''ICPT''. As of December 31, 2018, there were 29,693,876 shares of our common stock issued and outstanding and approximately 316 stockholders of record. A significantly larger number of stockholders may hold their shares in ''street name'' through banks, brokers and other nominees. The number of stockholders of record does not include stockholders who hold their shares in ''street name.''

Stock Price Performance Graph

The following graph compares the cumulative total stockholder return for our common stock to the cumulative total stockholder return for the Nasdaq Composite Index and the Nasdaq Biotechnology Index, in each case, for the period from December 31, 2013 through December 31, 2018. The graph assumes an initial investment of $100 in our common stock at the closing price of $68.28 on December 31, 2013 and in the Nasdaq Composite Index and the Nasdaq Biotechnology Index on December 31, 2013 and the reinvestment of dividends. The stock performance shown below is not intended to forecast or be indicative of the possible future performance of our common stock, and we do not make or endorse any predications as to future stockholder returns. The following stock performance information shall not be deemed to be ''soliciting material,'' ''filed'' with the U.S. Securities and Exchange Commission (the ''SEC''), incorporated by reference into any filing under the Securities Act of 1933, as amended (the ''Securities Act''), or the Securities Exchange Act of 1934, as amended (the ''Exchange Act''), or subject to the liabilities of Section 18 of the Exchange Act, except to the extent that we specifically incorporate it by reference into a document filed under the Securities Act or the Exchange Act.

Comparison of Cumulative Total Return
Among Intercept Pharmaceuticals, Inc., the Nasdaq Composite Index and the Nasdaq Biotechnology Index



$100 investment in stock or index	December 31, 2013	2014	2015	2016	2017	2018
Intercept Pharmaceuticals, Inc.	$100.00	$228.47	$218.73	$159.12	$ 85.56	$147.61
Nasdaq Composite Index	$100.00	$114.75	$122.74	$133.62	$173.22	$168.30
Nasdaq Biotechnology Index	$100.00	$134.40	$150.22	$118.15	$143.71	$130.97

Dividend Policy

We have never declared or paid any cash dividends on our common stock, and we do not anticipate paying any cash dividends in the foreseeable future.

Recent Sales of Unregistered Securities

Not applicable.

Issuer Purchases of Equity Securities

The following table provides certain information with respect to purchases of our common stock during the three months ended December 31, 2018.

Period	Total Number of Shares Purchased[1]	Average Price Paid per Share	Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs	Maximum Number (or Approximate Dollar Value) of Shares that May Yet Be Purchased Under the Plans or Programs
October 1, 2018 through October 31, 2018	3,748	$125.99	—	—
November 1, 2018 through November 30, 2018	2,273	$109.70	—	—
December 1, 2018 through December 31, 2018	—	—	—	—
Total	6,021	$119.84	—	—

(1) Represents shares of common stock withheld to satisfy taxes associated with the vesting of restricted stock awards.

Item 6. Selected Financial Data

The selected consolidated financial data set forth below should be read together with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our audited consolidated financial statements and accompanying notes included elsewhere in this Annual Report on Form 10-K. The selected consolidated financial data in this section are not intended to replace our audited consolidated financial statements and accompanying notes. Our historical results are not necessarily indicative of our future results.

The selected consolidated statements of operations data for the years ended December 31, 2018, 2017 and 2016 and the selected consolidated balance sheet data as of December 31, 2018 and 2017 have been derived from our audited consolidated financial statements and accompanying notes included elsewhere in this Annual Report on Form 10-K. The selected consolidated statements of operations data for the years ended December 31, 2015 and 2014 and the selected consolidated balance sheet data as of December 31, 2016, 2015 and 2014 have been derived from our audited consolidated financial statements and accompanying notes that are not included in this Annual Report on Form 10-K.

	Years Ended December 31,				
	2018	2017	2016	2015	2014
	(in thousands, except per share data)				
Consolidated Statement of Operations Data:					
Revenue:					
Product revenue, net	$ 177,782	$ 129,175	$ 18,169	$ —	$ —
Licensing revenue	2,022	1,781	6,782	2,782	1,742
Total revenues	179,804	130,956	24,951	2,782	1,742
Operating expenses:					
Cost of sales	2,519	1,371	—	—	—
Selling, general and administrative	255,474	273,698	273,596	119,242	34,601
Research and development	207,301	191,499	153,893	112,696	80,311
Total operating expenses	465,294	466,568	427,489	231,938	114,912
Operating loss	(285,490)	(335,612)	(402,538)	(229,156)	(113,170)
Total other income (expense), net[(1)]	(23,752)	(24,755)	(10,292)	2,727	(170,056)
Net loss	$(309,242)	$(360,367)	$(412,830)	$(226,429)	$(283,226)
Net loss per common and potential common share, basic and diluted	$ (10.86)	$ (14.38)	$ (16.74)	$ (9.56)	$ (13.63)
Weighted average common and potential common shares outstanding, basic and diluted	28,464	25,054	24,663	23,694	20,784

(1) For the year ended December 31, 2014, includes a $170.8 million non-cash expense related to the revaluation of certain previously outstanding warrants.

	December 31,				
	2018	2017	2016	2015	2014
			(in thousands)		
Consolidated Balance Sheet Data:					
Cash, cash equivalents and investment debt securities	$ 436,160	$ 414,917	$ 689,385	$ 628,055	$ 239,724
Total assets	509,167	484,347	739,253	655,758	254,149
Accounts payable, accrued expenses and other liabilities	105,109	94,777	65,551	45,591	13,459
Long-term debt[(1)]	371,250	355,677	341,356	—	—
Accumulated deficit	(1,778,785)	(1,469,543)	(1,108,460)	(695,630)	(469,202)
Total stockholders' equity	19,130	16,386	314,932	602,149	230,891

(1) Reflects $460.0 million aggregate principal amount of Convertible Notes, less unamortized debt discount and unamortized debt issuance costs as of December 31, 2018, 2017 and 2016. See Note 8 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K for further information regarding the Convertible Notes.

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

You should read the following discussion and analysis together with our audited consolidated financial statements and accompanying notes included elsewhere in this Annual Report on Form 10-K. This discussion and analysis contains forward-looking statements, which involve risks and uncertainties. As a result of many factors, such as those described under "Cautionary Note Regarding Forward-Looking Statements," "Risk Factors" and elsewhere in this Annual Report on Form 10-K, our actual results may differ materially from those anticipated in these forward-looking statements.

Overview

We are a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat progressive non-viral liver diseases with high unmet medical need utilizing our proprietary bile acid chemistry. Our first marketed product, Ocaliva® (obeticholic acid or "OCA"), is an farnesoid X receptor ("FXR") agonist approved in the United States, the European Union and several other jurisdictions for the treatment of primary biliary cholangitis ("PBC") in combination with ursodeoxycholic acid ("UDCA") in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA. In addition to commercializing OCA for PBC under the Ocaliva brand name, we are currently developing OCA for multiple indications, including nonalcoholic steatohepatitis ("NASH"). We are also developing several other product candidates in various stages of clinical and preclinical development. We believe that OCA and our other product candidates have the potential to treat orphan and other more prevalent liver diseases such as NASH for which there are currently limited therapeutic options.

Ocaliva was approved for PBC by the U.S. Food and Drug Administration ("FDA") in May 2016 under the accelerated approval pathway. We commenced sales and marketing of Ocaliva in the United States shortly after receiving approval, and Ocaliva is now available to U.S. patients primarily through a network of specialty pharmacy distributors. Ocaliva received conditional approval for PBC from the European Commission in December 2016 and we commenced our European commercial launch in January 2017. We have submitted dossiers and obtained, or are otherwise pursuing, reimbursement from a number of national authorities in Europe. Since January 2017, Ocaliva has also received regulatory approval in several of our target markets outside the United States and Europe, including Canada, Israel and Australia, and we are pursuing marketing approval of Ocaliva for PBC in our other international target markets. Ocaliva received orphan drug designation in both the United States and the European Union for the treatment of PBC.

Our lead product candidate is OCA for the potential treatment of NASH. In February 2019, we announced topline results from the planned 18-month interim analysis of our pivotal Phase 3 clinical trial of OCA in patients with liver fibrosis due to NASH, known as the REGENERATE trial. In the primary efficacy analysis, once-daily OCA 25 mg met the primary endpoint agreed with the FDA of fibrosis improvement by at least one stage with no worsening of NASH at the planned 18-month interim analysis and adverse events were generally mild to moderate in severity and the most common were consistent with the known profile of OCA. OCA also achieved the primary endpoint in a Phase 2b clinical trial for the treatment of NASH completed in late July 2014, known as the FLINT trial, which was sponsored by the U.S. National Institute of Diabetes and Digestive and Kidney Diseases, a part of the National Institutes of Health. OCA has received breakthrough therapy designation from the FDA for the treatment of NASH patients with liver fibrosis. We currently intend to file for approval of OCA for NASH in the United States and Europe in the second half of 2019. We also continue to work towards expanding our overall NASH development program with additional trials and studies, including our ongoing Phase 3 trial in NASH patients with compensated cirrhosis, known as the REVERSE trial.

As part of our product development activities, we expect to continue to invest in research of OCA for other progressive non-viral liver diseases beyond PBC and NASH. We also intend to study OCA in combination with bezafibrate, a pan-peroxisome proliferator-activated receptor ("PPAR") agonist, in patients with PBC and potentially other liver diseases. In addition, we have a pipeline of additional compounds in early stages of research and development.

Recent Developments

Phase 3 REGENERATE Trial Topline Results

In February 2019, we announced topline results from our pivotal Phase 3 clinical trial of OCA in patients with liver fibrosis due to NASH, known as the REGENERATE trial. In the primary efficacy analysis, once-daily OCA 25 mg met, with statistical significance, the primary endpoint agreed with the FDA of fibrosis improvement by at least one stage with no worsening of NASH (defined as no worsening of hepatocellular ballooning, no worsening of lobular inflammation and no worsening of steatosis) at the planned 18-month analysis and adverse events were generally mild to moderate in severity and the most common were consistent with the known profile of OCA. Although a numerically greater proportion of patients in both OCA treatment arms compared to placebo achieved the primary endpoint of NASH resolution with no worsening of liver fibrosis in the primary efficacy analysis, this result did not reach statistical significance. NASH resolution is defined as the overall histopathologic interpretation of (i) no fatty liver disease or (ii) fatty liver disease (simple or isolated steatosis) without steatohepatitis AND a nonalcoholic fatty liver disease activity score of 0 for ballooning and 0-1 for inflammation. As agreed with the FDA, in order for the primary objective to be met, the study was required to achieve one of the two primary endpoints. We currently intend to file for approval of OCA for NASH in the United States and Europe in the second half of 2019. REGENERATE is planned to continue through clinical outcomes in order to confirm clinical benefit. The end-of-study analysis will evaluate the effect of OCA on mortality and liver-related clinical outcomes, as well as its long-term safety.

Bezafibrate Transaction

In December 2018, we entered into an agreement (the ''Aralez Agreement'') with Aralez Pharmaceuticals Canada Inc. (''Aralez''), pursuant to which we acquired (i) Aralez's license to develop and commercialize bezafibrate in the United States (as amended and restated in connection therewith, the ''Bezafibrate License''), (ii) Aralez's investigational new drug application on file with the FDA and other associated regulatory documentation and (iii) a non-exclusive license to certain of Aralez's intellectual property. Pursuant to the Aralez Agreement, we paid $9.0 million to Aralez in connection with the closing of the transactions contemplated thereby in December 2018 and are obligated to make a $2.0 million milestone payment to Aralez based on the occurrence of specified regulatory-related events. Bezafibrate, a PPAR agonist that has been studied in PBC, is not approved in the U.S. for any indication. We intend to evaluate the efficacy, safety and tolerability of bezafibrate in combination with OCA in patients with PBC in a Phase 2 study, with the longer-term goal of developing and seeking regulatory approval for a fixed dose combination regimen in this indication and potentially other liver diseases. Pursuant to the Bezafibrate License, we are also obligated to make a $2.5 million milestone payment based on the occurrence of specified regulatory-related events with respect to such a combination product, as well as mid-single digit percentage royalty payments based on the net sales of such a combination product.

Capital Markets Activities During the Period Under Review

In April 2018, we issued and sold (i) 2,695,313 shares of common stock in a registered public offering (including 351,563 shares issued and sold upon the exercise in full of the underwriters' option to purchase additional shares), at a price to the public of $64.00 per share (the ''Public Offering'') and (ii) 1,562,500 shares of common stock (the ''Private Placement Shares'') in a concurrent private placement (the ''Concurrent Private Placement'') exempt from the registration requirements of the Securities Act, at a purchase price per share equivalent to the price to the public set in the Public Offering and pursuant to a securities purchase agreement (the ''Securities Purchase Agreement'') that we entered into with the purchasers in the Concurrent Private Placement (the ''Private Placement Purchasers''). Pursuant to the Securities Purchase Agreement, we granted to the Private Placement Purchasers certain registration rights requiring us, upon request of the Private Placement Purchasers (and/or certain affiliate transferees thereof) on or after June 5, 2018 and subject to certain terms and conditions, to register the resale by such Private Placement Purchasers (and/or such affiliates) of the Private Placement Shares held by them. We received net proceeds from the Public Offering and the Concurrent Private Placement of approximately $261.4 million, after deducting underwriting discounts, commissions and estimated offering expenses of approximately $11.1 million.

In July 2016, we issued and sold $460.0 million aggregate principal amount of 3.25% Convertible Senior Notes due 2023 (the ''Convertible Notes'') in a registered public offering. We received net proceeds from the sale of the Convertible Notes of approximately $447.6 million, after deducting underwriting discounts and estimated offering expenses of approximately $12.4 million, and used approximately $38.4 million of such net proceeds to fund the cost of the Capped Call Transactions (as defined below). In connection with the pricing of the Convertible Notes and the underwriters' exercise of their over-allotment option in full, we entered into capped call transactions (collectively, the ''Capped Call Transactions''). The Capped Call Transactions are expected generally to reduce the potential dilution with respect to our common stock and/or offset the cash payments we would be required to make in excess of the principal amount of converted Convertible Notes, as the case may be, upon conversion of the Convertible Notes in the event that the market price per share of our common stock, as measured under the terms of the Capped Call Transactions, is greater than the strike price of the Capped Call Transactions, which initially corresponds to the conversion price of the Convertible Notes and is subject to anti-dilution adjustments generally similar to those applicable to the conversion rate of the Convertible Notes. The cap price of the Capped Call Transactions is initially $262.2725 per share, and is subject to certain adjustments under the terms of the Capped Call Transactions. If, however, the market price per share of our common stock, as measured under the terms of the Capped Call Transactions, exceeds the cap price of the Capped Call Transactions, there would nevertheless be dilution and/or there would not be an offset of such potential cash payments, in each case, upon conversion of the Convertible Notes to the extent that such market price exceeds the cap price of the Capped Call Transactions.

Financial Overview

Revenue

We commenced our commercial launch of Ocaliva for the treatment of PBC in the United States in June 2016. In December 2016, the European Commission granted conditional approval for Ocaliva for the treatment of PBC and we commenced our European commercial launch in January 2017. Since January 2017, Ocaliva has also received regulatory approval in several of our target markets outside the United States and Europe, including Canada, Israel and Australia. We sell Ocaliva to a limited number of specialty pharmacies which dispense the product directly to patients. The specialty pharmacies are referred to as our customers.

Effective January 1, 2018, we began recognizing revenue under Accounting Standards Codification (''ASC'') Topic 606, *Revenue from Contracts with Customers* (''ASC 606''). The core principle of this revenue standard is that a company should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the company expects to be entitled in exchange for those goods or services. The following five steps are applied to achieve that core principle:

- Step 1: Identify the contract with the customer
- Step 2: Identify the performance obligations in the contract
- Step 3: Determine the transaction price
- Step 4: Allocate the transaction price to the performance obligations in the contract
- Step 5: Recognize revenue when the company satisfies a performance obligation

Product Revenue, Net

We provide the right of return to our customers for unopened product for a limited time before and after its expiration date. Prior to July 2017, given our limited sales history for Ocaliva and the inherent uncertainties in estimating product returns, we determined that the shipments of Ocaliva made to our customers did not meet the criteria for revenue recognition at the time of shipment. Accordingly, we recognized revenue when the product was sold through by our customers, provided all other revenue recognition criteria were met. We invoiced our customers upon shipment of Ocaliva to them and recorded accounts receivable, with a corresponding liability for deferred revenue equal to the gross invoice price. We then recognized revenue when Ocaliva was sold through as specialty pharmacies dispensed product directly to the patients (sell-through basis). We re-evaluated our revenue recognition policy in the third quarter of 2017, which included the accumulation and review of customer-related transactions since our commercial launch in the second quarter of 2016. We concluded we had accumulated sufficient data to reasonably estimate product

returns and, therefore, began to recognize revenue at the time of shipment to our customers (sell-in basis). During the third quarter of 2017, we recorded an adjustment related to this change in estimate to recognize previously deferred revenue. The net effect was an increase in net sales of Ocaliva of $4.1 million for the year ended December 31, 2017. We also established a new reserve of $0.7 million during 2017 related to future returns from our customers.

Under ASC 606, we have written contracts with each of our customers that have a single performance obligation — to deliver products upon receipt of a customer order — and these obligations are satisfied when delivery occurs and the customer receives Ocaliva. We evaluate the creditworthiness of each of our customers to determine whether collection is reasonably assured. We estimate variable revenue by calculating gross product revenues based on the wholesale acquisition cost that we charge our customers for Ocaliva, and then estimating our net product revenues by deducting (i) trade allowances, such as invoice discounts for prompt payment and customer fees, (ii) estimated government rebates and discounts related to Medicare, Medicaid and other government programs, and (iii) estimated costs of incentives offered to certain indirect customers including patients.

We recognized net sales of Ocaliva of $177.8 million, $129.2 million and $18.2 million for the years ended December 31, 2018, 2017 and 2016, respectively.

Licensing Revenue

In March 2011, we entered into an exclusive license agreement (the ‘‘Original Sumitomo Agreement’’) with Sumitomo Dainippon Pharma Co., Ltd. (‘‘Sumitomo Dainippon’’), pursuant to which we granted to Sumitomo Dainippon an exclusive license to research, develop and commercialize OCA for the treatment of PBC and NASH in Japan and China (excluding Taiwan) and an option to research, develop and commercialize OCA in certain countries outside of such territories (the ‘‘Country Option’’). We received an upfront payment from Sumitomo Dainippon of $15.0 million under the terms of the Original Sumitomo Agreement. In May 2014, Sumitomo Dainippon exercised the Country Option in part to add Korea as part of its licensed territories and paid us a $1.0 million upfront fee in connection therewith. In February 2018, we and Sumitomo Dainippon entered into Amendment No. 3 (the ‘‘Sumitomo Amendment’’) to the Original Sumitomo Agreement (as amended, the ‘‘Sumitomo Agreement’’), pursuant to which (i) Sumitomo Dainippon agreed to return the rights to develop and commercialize OCA in Japan and Korea and waived its rights to the Country Option, (ii) we agreed to forego any further milestone or royalty payments relating to the development and commercialization of OCA in Japan and Korea and (iii) certain milestone payment obligations with respect to the development and commercialization of OCA were adjusted. In addition, we and Sumitomo Dainippon agreed that if certain clinical development milestones in China are not met by December 31, 2020, Sumitomo Dainippon may choose either to make a milestone payment to us or terminate the Sumitomo Agreement. Sumitomo Dainippon may also terminate the Sumitomo Agreement in its entirety or on an indication-by-indication basis at any time upon 90 days' written notice. As of December 31, 2018, we had achieved $6.0 million of development milestones under the Sumitomo Agreement. We may be eligible to receive additional milestone payments under the Sumitomo Agreement in an aggregate amount of up to approximately $23.0 million based on the occurrence of certain clinical trial and regulatory-related events and tiered royalty payments up to the mid-twenties in percentage terms based on net sales of OCA products in China (excluding Taiwan).

For accounting purposes, the upfront payments were recorded as deferred revenue and amortized over time and milestone payments are recognized once earned. For the years ended December 31, 2018, 2017 and 2016, we recognized $2.0 million, $1.8 million and $6.8 million, respectively, in licensing revenue related to milestone payments and/or the amortization of the upfront payments under the Sumitomo Agreement. Included in licensing revenue for the year ended December 31, 2018 is $0.4 million related to the accelerated recognition, as a result of the Sumitomo Amendment, of the remaining portion of deferred revenue associated with the $1.0 million upfront payment that we received under the Original Sumitomo Agreement in connection with Sumitomo Dainippon's exercise of the Country Option with respect to Korea. We anticipate that we will recognize additional revenue of approximately $2.4 million through June 2020, related to the amortization of upfront payments under the Sumitomo Agreement.

Selling, General and Administrative Expenses

We have incurred and expect to continue to incur significant selling, general and administrative expenses as a result of, among other initiatives, the launch and commercialization of Ocaliva for PBC in the United States, Europe and our other target markets, the preparation for the potential commercialization of OCA for NASH, if approved, and our other future approved products, if any, and the build-out of our general and administrative infrastructure in the United States and abroad.

Research and Development Expenses

Since our inception, we have focused significant resources on our research and development activities, including conducting preclinical studies and clinical trials, pursuing regulatory approvals and engaging in other product development activities. We recognize research and development expenses as they are incurred.

We have incurred and expect to continue to incur significant research and development expenses as a result of, among other initiatives, our clinical development programs for OCA for PBC and NASH, our other earlier stage research programs and our regulatory approval efforts.

Results of Operations

Comparison of the Years Ended December 31, 2018 and 2017

The following table summarizes our results of operations for the years ended December 31, 2018 and 2017:

	Years Ended December 31,	
	2018	**2017**
	(in thousands)	
Revenue:		
Product revenue, net	$ 177,782	$ 129,175
Licensing revenue	2,022	1,781
Total revenue	179,804	130,956
Operating expenses:		
Cost of sales	2,519	1,371
Selling, general and administrative	255,474	273,698
Research and development	207,301	191,499
Total operating expenses	465,294	466,568
Other income (expense):		
Interest expense	(30,523)	(29,271)
Other income, net	6,771	4,516
	(23,752)	(24,755)
Net loss	$(309,242)	$(360,367)

Revenues

Product revenue, net was $177.8 million and $129.2 million for the years ended December 31, 2018 and 2017, respectively. For the years ended December 31, 2018 and 2017, product revenue, net was comprised of U.S. Ocaliva net sales of $140.8 million and $115.8 million, respectively, and ex-U.S. Ocaliva net sales of $37.0 million and $13.4 million, respectively. We commenced our commercial launch of Ocaliva for the treatment of PBC in the United States and certain European countries in June 2016 and January 2017, respectively. Since January 2017, Ocaliva has also received regulatory approval in several of our target markets outside the United States and Europe, including Canada, Israel and Australia. Included in product revenue, net for the year ended December 31, 2017 is $4.1 million of previously deferred revenue recognized in connection with our adoption of a sell-in basis revenue recognition policy in the third quarter of 2017. For the years ended December 31, 2018 and 2017, licensing revenue was $2.0 million and $1.8 million, respectively, in each case, related to the amortization of upfront payments under the Sumitomo Agreement.

Cost of sales

Cost of sales was $2.5 million and $1.4 million for the years ended December 31, 2018 and 2017, respectively. Prior to the FDA's approval of Ocaliva in May 2016, we expensed costs related to the manufacturing and buildup of our Ocaliva commercial launch supplies as research and development expenses. As a result, our cost of sales for the years ended December 31, 2018 and 2017 consisted primarily of packaging and labeling expenses.

Selling, general and administrative expenses

Selling, general and administrative expenses were $255.5 million and $273.7 million for the years ended December 31, 2018 and 2017, respectively. The $18.2 million net decrease between periods primarily reflects the inclusion in selling, general and administrative expenses for the year ended December 31, 2017 of $9.8 million of expenses incurred in connection with our termination in December 2017 of a lease agreement relating to office space at 55 Hudson Yards and $3.9 million of restructuring-related charges.

Research and development expenses

Research and development expenses were $207.3 million and $191.5 million for the years ended December 31, 2018 and 2017, respectively, representing a net increase of $15.8 million. The net increase in research and development expenses primarily reflects $9.0 million that we paid to Aralez in December 2018 pursuant to the Aralez Agreement, as well as an increase in OCA research and development activities of approximately $16.8 million, partially offset by a decrease of approximately $12.1 million in compensation-related costs, which includes $1.3 million of restructuring-related charges incurred in the year ended December 31, 2017.

Interest expense

Interest expense was $30.5 million and $29.3 million for the years ended December 31, 2018 and 2017, respectively, in each case, related to the Convertible Notes.

Other income, net

Other income, net was $6.8 million and $4.5 million for the years ended December 31, 2018 and 2017, respectively. Such income is primarily attributable to interest income earned on cash, cash equivalents and investment debt securities.

Income taxes

For the years ended December 31, 2018 and 2017, no income tax expense or benefit was recognized. Our deferred tax assets are comprised primarily of net operating loss carryforwards. We maintain a full valuation allowance on our deferred tax assets since we have not yet achieved sustained profitable operations. As a result, we have not recorded any income tax benefit since our inception.

Comparison of the Years Ended December 31, 2017 and 2016

The following table summarizes our results of operations for the years ended December 31, 2017 and 2016:

	Years Ended December 31,	
	2017	**2016**
	(in thousands)	
Revenue:		
Product revenue, net	$ 129,175	$ 18,169
Licensing revenue	1,781	6,782
Total revenue	130,956	24,951
Operating expenses:		
Cost of sales	1,371	—
Selling, general and administrative	273,698	273,596
Research and development	191,499	153,893
Total operating expenses	466,568	427,489
Other income (expense):		
Interest expense	(29,271)	(14,196)
Other income, net	4,516	3,904
	(24,755)	(10,292)
Net loss	$(360,367)	$(412,830)

Revenues

Product revenue, net was $129.2 million and $18.2 million for the years ended December 31, 2017 and 2016, respectively. For the year ended December 31, 2017, product revenue, net was comprised of U.S. Ocaliva net sales of $115.8 million and ex-U.S. Ocaliva net sales of $13.4 million. For the year ended December 31, 2016, product revenue, net was comprised entirely of U.S. Ocaliva net sales. We commenced our commercial launch of Ocaliva for the treatment of PBC in the United States and certain European countries in June 2016 and January 2017, respectively. Included in product revenue, net for the year ended December 31, 2017 is $4.1 million of previously deferred revenue recognized in connection with our adoption of a sell-in basis revenue recognition policy in the third quarter of 2017. For the years ended December 31, 2017 and 2016, licensing revenue was $1.8 million and $6.8 million, respectively, related to the amortization of upfront payments and, in 2016, recognition of a milestone payment, in each case, under the Sumitomo Agreement.

Cost of sales

Cost of sales was $1.4 million and $0 for the years ended December 31, 2017 and 2016, respectively. Prior to the FDA's approval of Ocaliva, we expensed costs related to the manufacturing and buildup of our Ocaliva commercial launch supplies as research and development expenses. As a result, our cost of sales for the year ended December 31, 2017 consisted primarily of packaging and labeling expenses.

Selling, general and administrative expenses

Selling, general and administrative expenses were $273.7 million and $273.6 million for the years ended December 31, 2017 and 2016, respectively. The $0.1 million net increase between periods primarily reflects an increase of approximately $24.1 million in personnel-related costs, which includes $3.9 million of restructuring-related charges incurred in the year ended December 31, 2017, and an increase of $17.4 million related to commercialization, market research and medical affairs activities, as well as $9.8 million of expenses incurred in connection with our termination in December 2017 of a lease agreement relating to office space at 55 Hudson Yards, partially offset by the inclusion in selling, general and administrative expenses for the year ended December 31, 2016 of a payment of $45.0 million in connection with the settlement of a purported securities class action lawsuit in 2016 and related legal expenses of $3.4 million.

Research and development expenses

Research and development expenses were $191.5 million and $153.9 million for the years ended December 31, 2017 and 2016, respectively, representing a net increase of $37.6 million. The net increase in research and development expenses primarily reflects an increase in OCA research and development activities of approximately $34.9 million and an increase of $2.2 million of compensation-related costs, which includes $1.3 million of restructuring-related charges incurred in the year ended December 31, 2017.

Interest expense

Interest expense was $29.3 million and $14.2 million for the years ended December 31, 2017 and 2016, respectively, in each case, related to the Convertible Notes issued in July 2016.

Other income, net

Other income, net was $4.5 million and $3.9 million for the years ended December 31, 2017 and 2016, respectively. The $0.6 million increase between periods is primarily attributable to higher cash and investment balances resulting from the net proceeds from the Convertible Notes issued in July 2016.

Income Taxes

For the years ended December 31, 2017 and 2016, no income tax expense or benefit was recognized. Our deferred tax assets are comprised primarily of net operating loss carryforwards. We maintain a full valuation allowance on our deferred tax assets since we have not yet achieved sustained profitable operations. As a result, we have not recorded any income tax benefit since our inception.

In December 2017, the United States enacted the Tax Cuts and Jobs Act of 2017, which significantly changed U.S. tax law, including by implementing a reduction in the corporate tax rate to 21%, moving from a worldwide tax system to a territorial system and imposing new or additional limitations on the deductibility of interest expense and executive compensation. Upon enactment of this legislation, we remeasured our deferred tax assets and liabilities and continued to maintain a full valuation allowance as of December 31, 2017. As a result of adopting the legislation, there was no tax expense recorded in our consolidated financial statements.

Liquidity and Capital Resources

Cash Flows

The following table sets forth the significant sources and uses of cash for the periods indicated:

	Years Ended December 31,		
	2018	2017	2016
		(in thousands)	
Net cash provided by (used in):			
Operating activities	$(240,714)	$(265,402)	$(342,441)
Investing activities	(48,070)	287,775	(60,135)
Financing activities	263,545	2,838	414,382
Effect of exchange rate changes	(1,526)	1,127	(873)
Net (decrease) increase in cash and cash equivalents	$ (26,765)	$ 26,338	$ 10,933

Operating Activities. Net cash used in operating activities of $240.7 million during the year ended December 31, 2018 was primarily a result of our $309.2 million net loss and a net decrease in operating assets and liabilities of $2.8 million, partially offset by $49.9 million in stock-based compensation, $14.0 million for accretion of the discount on the Convertible Notes, and $4.6 million of depreciation.

Net cash used in operating activities of $265.4 million during the year ended December 31, 2017 was primarily a result of our $360.4 million net loss, partially offset by a net increase in operating assets and liabilities of $14.6 million, $57.0 million in stock-based compensation, $12.9 million for accretion of the discount on the Convertible Notes, $4.6 million of depreciation and $3.4 million for amortization of investment premium.

Net cash used in operating activities of $342.4 million during the year ended December 31, 2016 was primarily a result of our $412.8 million net loss, partially offset by a net increase in operating assets and

liabilities of $8.4 million, $46.2 million in stock-based compensation, $6.2 million for accretion of the discount on the Convertible Notes, $4.9 million for amortization of investment premium and $3.8 million of depreciation.

Investing Activities. For the year ended December 31, 2018, net cash used in investing activities primarily reflects the purchase of investment debt securities of $436.1 million, partially offset by the sale of investment debt securities of $388.2 million.

For the year ended December 31, 2017, net cash provided by investing activities primarily reflects the sale of investment debt securities of $529.3 million, partially offset by the purchase of investment debt securities of $231.1 million and $10.4 million of capital expenditures primarily related to our offices.

For the year ended December 31, 2016, net cash used in investing activities primarily reflects the purchase of investment debt securities of $511.5 million, partially offset by the sale of investment debt securities of $456.5 million and $5.1 million of capital expenditures primarily related to our offices.

Financing Activities. Net cash provided by financing activities in the year ended December 31, 2018 consisted primarily of net proceeds of approximately $261.4 million from the Public Offering and Concurrent Private Placement in April 2018 and $2.2 million from the exercise of options to purchase common stock net of payments of employee withholding taxes related to stock-based awards.

Net cash provided by financing activities in the year ended December 31, 2017 consisted primarily of $2.8 million from the exercise of options to purchase common stock.

Net cash provided by financing activities in the year ended December 31, 2016 consisted primarily of net proceeds of approximately $447.6 million from the Convertible Notes issued in July 2016 and $5.2 million from the exercise of options to purchase common stock, partially offset by payments of $38.4 million to fund the cost of the Capped Call Transactions related to the Convertible Notes.

Future Funding Requirements

As of December 31, 2018, we had $436.2 million in cash, cash equivalents and investment debt securities. We currently expect to continue to incur significant operating expenses in the fiscal year ending December 31, 2019. These expenses are planned to support, among other initiatives, the continued commercialization of Ocaliva for PBC in the United States and our other markets, our continued clinical development of OCA for PBC and NASH and our other earlier stage research programs. Although we believe that our existing capital resources, together with our net sales of Ocaliva for PBC, will be sufficient to fund our anticipated operating requirements for the next twelve months, we may need to raise additional capital to fund our operating requirements beyond that period. Furthermore, in light of the numerous risks and uncertainties associated with pharmaceutical product development and commercialization, any delays in, or unanticipated costs associated with, our development, regulatory or commercialization efforts could significantly increase the amount of capital required by us to fund our operating requirements. Accordingly, we may seek to access the public or private capital markets whenever conditions are favorable, even if we do not have an immediate need for additional capital at that time. Our forecast regarding the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results, including the costs to maintain our currently planned operations, could vary materially.

Our forecasts regarding the period of time that our existing capital resources will be sufficient to meet our operating requirements and the timing of our future funding requirements, both near and long-term, will depend on a variety of factors, many of which are outside of our control. Such factors include, but are not limited to:

- our ability to successfully commercialize Ocaliva for PBC;
- our ability to maintain our regulatory approval of Ocaliva for PBC in the United States, Europe, Canada, Israel, Australia and other jurisdictions in which we have or may receive marketing authorization;

- the initiation, timing, cost, conduct, progress and results of our research and development activities, preclinical studies and clinical trials, including any issues, delays or failures in identifying patients, enrolling patients, treating patients, meeting specific endpoints in the jurisdictions in which we intend to seek approval or completing and timely reporting the results of our NASH or PBC clinical trials;
- our ability to timely and cost-effectively file for and obtain regulatory approval of our product candidates, including OCA for NASH, in the United States, Europe and our other target markets;
- conditions that may be imposed by regulatory authorities on our marketing approvals for our products and product candidates, such as the need for clinical outcomes data (and not just results based on achievement of a surrogate endpoint), and any related restrictions, limitations and/or warnings contained in the label of any of our products or product candidates;
- any potential side effects associated with Ocaliva for PBC, OCA for NASH or our other product candidates that could delay or prevent approval, require that an approved product be taken off the market, require the inclusion of safety warnings or precautions or otherwise limit the sale of such product or product candidate;
- our ability to establish and maintain relationships with, and the performance of, third-party manufacturers, contract research organizations and other vendors upon whom we are substantially dependent for, among other things, the manufacture and supply of our products, including Ocaliva for PBC and, if approved, OCA for NASH, and our clinical trial activities;
- our ability to identify, develop and successfully commercialize our products and product candidates, including our ability to timely and successfully launch OCA for NASH, if approved;
- our ability to obtain and maintain intellectual property protection for our products and product candidates, including our ability to cost-effectively file, prosecute, defend and enforce any patent claims or other intellectual property rights;
- the size and growth of the markets for our products and product candidates and our ability to serve those markets;
- the degree of market acceptance of Ocaliva for PBC and, if approved, OCA for NASH or our other product candidates among physicians, patients and healthcare payors;
- the availability of adequate coverage and reimbursement from governmental and private healthcare payors for our products, including Ocaliva for PBC and, if approved, OCA for NASH, and our ability to obtain adequate pricing for such products;
- our ability to establish and maintain effective sales, marketing and distribution capabilities, either directly or through collaborations with third parties;
- competition from existing drugs or new drugs that become available;
- our ability to prevent system failures, data breaches or violations of data protection laws;
- costs and outcomes relating to any disputes, governmental inquiries or investigations, legal proceedings or litigation, including any securities, intellectual property, employment, product liability or other litigation;
- our collaborators' election to pursue research, development and commercialization activities;
- our ability to establish and maintain relationships with collaborators with development, regulatory and commercialization expertise;
- our need for and ability to generate or obtain additional financing;
- our estimates regarding future expenses, revenues and capital requirements and the accuracy thereof;
- our use of cash and short-term investments;

- our ability to acquire, license and invest in businesses, technologies, product candidates and products;
- our ability to attract and retain key personnel to manage our business effectively;
- our ability to manage the growth of our operations, infrastructure, personnel, systems and controls;
- our ability to obtain and maintain adequate insurance coverage;
- the impact of general U.S. and foreign economic, industry, market, regulatory or political conditions, including the potential impact of Brexit; and
- the other risks and uncertainties identified under the captions ''Risk Factors,'' ''Business'' and ''Management's Discussion and Analysis of Financial Condition and Results of Operations'' and elsewhere in this Annual Report on Form 10-K and in our other periodic filings filed with the SEC.

We have no committed external sources of funding and additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available to us, we may not be able to make scheduled debt payments on a timely basis, or at all, and may be required to delay, limit, reduce or cease our operations.

Public Offering and Concurrent Private Placement

In April 2018, we issued and sold an aggregate of 4,257,813 shares of common stock in the Public Offering and Concurrent Private Placement. We received net proceeds from the Public Offering and the Concurrent Private Placement of approximately $261.4 million, after deducting underwriting discounts, commissions and estimated offering expenses of approximately $11.1 million.

Convertible Notes and Capped Call Transactions

In July 2016, we issued and sold $460.0 million aggregate principal amount of the Convertible Notes. We received net proceeds from the sale of the Convertible Notes of approximately $447.6 million, after deducting underwriting discounts and estimated offering expenses of approximately $12.4 million, and used approximately $38.4 million of such net proceeds to fund the cost of the Capped Call Transactions that were entered into in connection with the issuance of the Convertible Notes. The Convertible Notes are senior unsecured obligations of ours, bear interest at a fixed rate of 3.25% per year (payable semi-annually on January 1 and July 1 of each year, beginning on January 1, 2017) and will mature on July 1, 2023, unless earlier repurchased, redeemed or converted.

The Convertible Notes were issued pursuant to an indenture, as supplemented by a first supplemental indenture, each dated as of July 6, 2016 (collectively, the ''Indenture''), by and between us and U.S. Bank National Association, as trustee. The Convertible Notes are convertible at the option of holders, under certain circumstances and during certain periods, into cash, shares of our common stock or a combination of cash and shares of our common stock, at our election. The initial conversion rate of the Convertible Notes is 5.0358 shares of our common stock per $1,000 principal amount of Convertible Notes, which is equivalent to an initial conversion price of approximately $198.58 per share of our common stock. The conversion rate is subject to adjustment upon the occurrence of certain events but will not be adjusted for any accrued and unpaid interest. If we undergo a fundamental change (as defined in the Indenture), holders may require us to repurchase for cash all or any portion of their Convertible Notes at a fundamental change repurchase price equal to 100% of the principal amount of the Convertible Notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date. In addition, if certain make-whole fundamental changes occur, we will, in certain circumstances, increase the conversion rate for any Convertible Notes converted in connection with such make-whole fundamental change. We may not redeem the Convertible Notes prior to July 6, 2021. We may redeem for cash all or part of the Convertible Notes, at our option, on or after July 6, 2021, under certain circumstances at a redemption price equal to 100% of the principal amount of the Convertible Notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date. The Indenture provides for customary events of default.

In connection with the pricing of the Convertible Notes and the underwriters' exercise of their over-allotment option in full, we entered into the Capped Call Transactions. The Capped Call Transactions are

expected generally to reduce the potential dilution with respect to our common stock and/or offset the cash payments we would be required to make in excess of the principal amount of converted Convertible Notes, as the case may be, upon conversion of the Convertible Notes in the event that the market price per share of our common stock, as measured under the terms of the Capped Call Transactions, is greater than the strike price of the Capped Call Transactions, which initially corresponds to the conversion price of the Convertible Notes and is subject to anti-dilution adjustments generally similar to those applicable to the conversion rate of the Convertible Notes. The cap price of the Capped Call Transactions is initially $262.2725 per share, and is subject to certain adjustments under the terms of the Capped Call Transactions. If, however, the market price per share of our common stock, as measured under the terms of the Capped Call Transactions, exceeds the cap price of the Capped Call Transactions, there would nevertheless be dilution and/or there would not be an offset of such potential cash payments, in each case, upon conversion of the Convertible Notes to the extent that such market price exceeds the cap price of the Capped Call Transactions.

Contractual Obligations

Our contractual obligations as of December 31, 2018 consisted primarily of obligations under the Convertible Notes, purchase obligations entered into in the normal course of business and lease agreements. The following table summarizes our material contractual obligations as of December 31, 2018 and the effect such obligations are expected to have on our liquidity and cash flows in future years:

	Payments Due By Period				
	Total	Less than 1 year	1 – 3 years	4 – 5 years	More than 5 years
			(in thousands)		
Contractual Obligations:					
Operating leases[1]	$ 29,931	$ 9,506	$12,967	$ 5,927	$1,531
Convertible Notes[2]	527,275	14,950	29,900	482,425	—
Purchase obligations[3]	29,802	20,030	7,426	2,341	5
Total	$587,008	$44,486	$50,293	$490,693	$1,536

(1) For a description of our material operating leases, see ‘‘Properties’’ above.

(2) Represents Convertible Notes due in 2023 (including future interest payments at a fixed rate of 3.25% per year).

(3) A ‘‘purchase obligation’’ is defined as an agreement to purchase goods or services that is enforceable and legally binding on us and that specifies all significant terms, including: fixed or minimum quantities to be purchased; fixed, minimum or variable price provisions; and the approximate timing of the transaction. The purchase obligation amounts do not represent the entire anticipated purchases in the future, but represent only those items for which we are contractually obligated as of December 31, 2018. We also purchase products and services as needed with no firm commitment. As a result, the amounts presented in the table above do not provide a reliable indicator of our expected future cash outflows. We have included as purchase obligations our commitments under agreements to the extent they are quantifiable and are not cancelable.

We enter into contracts in the normal course of business with contract research organizations for our clinical trials, contract manufacturing organizations for the manufacture and supply of our clinical and commercial product needs and other vendors for other research and development and commercial activities, as well as services and products for operating purposes. Our agreements generally provide for termination with notice. Such agreements are cancelable contracts are not included as purchase commitments.

Off-Balance Sheet Arrangements

As of December 31, 2018, we did not have any off-balance sheet arrangements.

Critical Accounting Policies and Estimates

Our management’s discussion and analysis of our financial condition and results of operations is based on our audited consolidated financial statements, which we have prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of our audited consolidated

financial statements requires us to make estimates and judgments that affect the reported amounts of assets and liabilities, the disclosure of assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. We evaluate these estimates and judgments on an ongoing basis. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Our actual results could differ from these estimates.

While our significant accounting policies are more fully described in Note 2 to our audited consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are the most critical for fully understanding and evaluating our financial condition and results of operations.

Revenue Recognition

Effective January 1, 2018, we began recognizing revenue under ASC 606 using the modified retrospective approach. The core principle of this revenue standard is that a company should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the company expects to be entitled in exchange for those goods or services. The following five steps are applied to achieve that core principle: (i) identify the contract with the customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract and (v) recognize revenue when the company satisfies a performance obligation.

Product Revenue, Net

We commenced our commercial launch of Ocaliva for the treatment of PBC in the United States in June 2016. In December 2016, the European Commission granted conditional approval for Ocaliva for the treatment of PBC and we commenced our European commercial launch in January 2017. Since January 2017, Ocaliva has also received regulatory approval in several of our target markets outside the United States and Europe, including Canada, Israel and Australia. We sell Ocaliva to a limited number of specialty pharmacies which dispense the product directly to patients. The specialty pharmacies are referred to as our customers.

We provide the right of return to our customers for unopened product for a limited time before and after its expiration date. Prior to July 2017, given our limited sales history for Ocaliva and the inherent uncertainties in estimating product returns, we determined that the shipments of Ocaliva made to our customers did not meet the criteria for revenue recognition at the time of shipment. Accordingly, we recognized revenue when the product was sold through by our customers, provided all other revenue recognition criteria were met. We invoiced our customers upon shipment of Ocaliva to them and recorded accounts receivable, with a corresponding liability for deferred revenue equal to the gross invoice price. We then recognized revenue when Ocaliva was sold through as specialty pharmacies dispensed product directly to the patients (sell-through basis). We re-evaluated our revenue recognition policy in the third quarter of 2017, which included the accumulation and review of customer-related transactions since our commercial launch in the second quarter of 2016. We concluded we had accumulated sufficient data to reasonably estimate product returns and, therefore, began to recognize revenue at the time of shipment to our customers (sell-in basis). During the third quarter of 2017, we recorded an adjustment related to this change in estimate to recognize previously deferred revenue. The net effect was an increase in net sales of Ocaliva of $4.1 million for the year ended December 31, 2017. We also established a new reserve of $0.7 million during 2017 related to future returns from our customers.

Under ASC 606, we have written contracts with each of our customers that have a single performance obligation — to deliver products upon receipt of a customer order — and these obligations are satisfied when delivery occurs and the customer receives Ocaliva. We evaluate the creditworthiness of each of our customers to determine whether collection is reasonably assured. We estimate variable revenue by calculating gross product revenues based on the wholesale acquisition cost that we charge our customers for Ocaliva, and then estimating our net product revenues by deducting (i) trade allowances, such as invoice discounts for prompt

payment and customer fees, (ii) estimated government rebates and discounts related to Medicare, Medicaid and other government programs, and (iii) estimated costs of incentives offered to certain indirect customers including patients.

Trade Allowances

We provide invoice discounts on Ocaliva sales to certain of our customers for prompt payment and record these discounts as a reduction to gross product revenues. These discounts are based on contractual terms.

Rebates and Discounts

We contract with the Centers for Medicare & Medicaid Services and other government agencies to make Ocaliva available to eligible patients. As a result, we estimate any rebates and discounts and deduct these estimated amounts from our gross product revenues at the time the revenues are recognized. Our estimates of rebates and discounts are based on the government mandated discounts, which are statutorily-defined and applicable to these government funded programs. These estimates are recorded in accounts payable, accrued expenses and other liabilities on our consolidated balance sheet.

Other Incentives

Other incentives that we offer to indirect customers include co-pay assistance cards provided by us for PBC patients who reside in states that permit co-pay assistance programs. Our co-pay assistance program is intended to reduce each participating patient's portion of the financial responsibility for Ocaliva purchase price to a specified dollar amount. We estimate the amount of co-pay assistance provided to eligible patients based on the terms of the program when product is dispensed by the specialty pharmacies to the patients. These estimates are based on redemption information provided by third-party claims processing organizations and are recorded in accounts payable, accrued expenses and other liabilities on our consolidated balance sheet.

Stock-Based Compensation

We account for stock-based compensation in accordance with ASC Topic 718, *Compensation — Stock Compensation*. We estimate the fair value of stock option awards using the Black-Scholes option pricing model on the date of the grant. The Black-Scholes option pricing model requires the use of assumptions, including with respect to stock price volatility, assumed dividend yield, the expected term of options and the risk-free interest rate, as described below:

- The expected volatility was estimated based on historical volatility information of publicly-traded peer companies. For the purpose of identifying peer companies, we consider characteristics such as industry, length of trading history, similar vesting terms and in-the-money option status.
- The assumed dividend yield is based on our expectation of not paying dividends for the foreseeable future.
- The expected term of options granted represents the period of time the options are expected to be outstanding and is based on the simplified method.
- The risk-free interest rate was based on the rate for U.S. Treasury securities at the date of grant with maturity dates approximately equal to the expected term of the award at the grant date.

Restricted stock unit awards and restricted stock awards without a market condition are valued based on the closing price of our common stock on the date of the grant. The fair value of time-based equity awards is recognized and amortized on a straight-line basis over the requisite service period of the award. We recognize stock-based compensation expense for options and other stock-based awards with performance conditions ratably over the performance period once the pre-defined performance-based criteria for vesting becomes probable. At the probable date, we record a cumulative expense catch-up, with remaining expense amortized over the remaining service period. Throughout the performance period, we re-assess the estimated performance and update the numbers of performance-based awards that we believe will ultimately vest. Upon the conclusion of the performance period, the performance level is measured to determine the ultimate level of shares that will vest. The fair value of awards with market conditions is estimated using the Monte Carlo simulation method and expense is recognized on a straight-line basis over the requisite service period of the

award. We recognize stock-based compensation for non-employees (other than non-employee directors) on a mark-to-market basis, which is updated on a quarterly basis. We account for all forfeitures when they occur. Ultimately, the actual expense recognized over the vesting period will be for only those shares that vest and are not forfeited.

We expect to continue to grant stock options and other stock-based awards and the impact of stock-based compensation may fluctuate in future periods due to changes in the value of our common stock, changes to our headcount and the number and value of awards granted.

Convertible Senior Notes

The Convertible Notes are accounted for in accordance with ASC Subtopic 470-20, *Debt with Conversion and Other Options*. ASC Subtopic 470-20 requires the issuer of convertible debt that may be settled in shares or cash upon conversion at the issuer's option, such as the Convertible Notes, to account for the liability (debt) and equity (conversion option) components separately. The value assigned to the debt component is the estimated fair value, as of the issuance date, of a similar debt instrument without the conversion option. The amount of the equity component (and resulting debt discount) is calculated by deducting the fair value of the liability component from the principal amount of the convertible debt instrument. The resulting debt discount is amortized as additional non-cash interest expense over the expected life of the notes utilizing the effective interest method. Although ASC 470-20 has no impact on our actual past or future cash flows, it requires us to record non-cash interest expense as the debt discount is amortized. For additional information, see Note 8 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Income Taxes

We utilize the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial statement carrying amounts and tax bases of assets and liabilities using enacted tax rates in effect for years in which the temporary differences are expected to reverse. We determine the need for a valuation allowance by assessing the probability of realizing deferred tax assets, taking into consideration all available positive and negative evidence, including historical operating results, expectations of future taxable income, carryforward periods available, various income tax strategies and other relevant factors. Significant judgment is required in making this assessment and to the extent future expectations change, we would have to assess the recoverability of our deferred assets at that time. At December 31, 2018 and 2017, we maintained a full valuation allowance on our deferred tax assets. At any one time our tax returns for numerous tax years are subject to examination by U.S. Federal, state, and foreign taxing jurisdictions. The impact of an uncertain tax position taken or expected to be taken on an income tax return must be recognized in our financial statements at the largest amount that is more likely than not to be sustained. An uncertain income tax position will not be recognized in our financial statements unless it is more likely than not to be sustained. At December 31, 2018 and 2017, we had no reserves for unrecognized tax benefits.

Recent Accounting Pronouncements

See Note 2 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K for a full description of recent accounting pronouncements including the respective expected dates of adoption and expected effects, if any, on our results of operations and financial condition.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. We currently do not hedge interest rate exposure. Because of the short-term maturities of our cash equivalents and investment debt securities, we do not believe that an increase in market rates would have any significant impact on the realized value of our investment debt securities. If a 10% change in interest rates were to have occurred on December 31, 2018, this change would not have had a material effect on the fair value of our investment portfolio as of that date.

We do not believe that our cash and cash equivalents and available-for-sale investments have significant risk of default or illiquidity. While we believe our cash, cash equivalents and available for sale 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 or more financial institutions that are in excess of federally insured limits.

We contract with CROs, investigational sites, suppliers, facilities, marketing firms and other vendors and suppliers in Europe and internationally. We are therefore subject to fluctuations in foreign currency rates in connection with these agreements. We do not hedge our foreign currency exchange rate risk.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations during the years ended December 31, 2018, 2017 or 2016.

Item 8. Financial Statements and Supplementary Data

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K and incorporated by reference herein. An index of those financial statements is set forth under Item 15. ''Exhibits and Financial Statement Schedules''.

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 Chief Executive Officer and Chief Financial Officer evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2018. The term ''disclosure controls and procedures,'' as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2018, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act, as a process designed by, or under the supervision of, the company's principal executive and principal financial officers and effected by the company's board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that: (i) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of our company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of our company's assets that could have a material effect on the financial statements.

All internal controls, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to consolidated financial statement preparation and presentation. Because of its inherent limitations, internal control over

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

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, assessed the effectiveness of our internal control over financial reporting as of December 31, 2018, based on criteria established in the Internal Control — Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on that assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2018.

Attestation Report of Independent Registered Public Accounting Firm

The effectiveness of our internal control over financial reporting as of December 31, 2018 has been audited by KPMG LLP, an independent registered public accounting firm, as stated in their report included elsewhere in this Annual Report on Form 10-K.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the quarter ended December 31, 2018 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

We have adopted a Global Code of Business Conduct as our ''code of ethics,'' as defined by regulations promulgated under the Securities Act of 1933, as amended, and the Securities Exchange Act of 1934, as amended, which applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. The Global Code of Business Conduct is available on our website at www.interceptpharma.com in the Investors & Media section under ''Corporate Governance.'' We intend to satisfy the disclosure requirement under Item 5.05 of Form 8-K regarding any future amendment to, or waiver from, a provision of the Global Code of Business Conduct that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions by posting such information on our website at www.interceptpharma.com in the Investors & Media section under ''Corporate Governance.'' The references to *www.interceptpharma.com* herein are inactive textual references only, and the information found on our internet website is not incorporated by reference into this Annual Report on Form 10-K or any other report we file with or furnish to the SEC.

The remainder of the information required by this item is incorporated by reference to our definitive proxy statement related to our 2019 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

Item 11. Executive Compensation

The information required by this item is incorporated by reference to our definitive proxy statement related to our 2019 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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

The information required by this item is incorporated by reference to our definitive proxy statement related to our 2019 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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

The information required by this item is incorporated by reference to our definitive proxy statement related to our 2019 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

Item 14. Principal Accounting Fees and Services

The information required by this item is incorporated by reference to our definitive proxy statement related to our 2019 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) 1. Index to Consolidated Financial Statements

2. Financial Statement Schedules

Financial statement schedules have been omitted from this Annual Report on Form 10-K because they are not applicable, not required or the information required is set forth in the audited consolidated financial statements or accompanying notes.

3. Exhibits

The exhibits filed or furnished as part of this Annual Report on Form 10-K are set forth in the Exhibit Index below, which is incorporated herein by reference.

Exhibit List

Exhibit Number	Exhibit Description	Incorporated herein by reference		
		Form†	Exhibit	Filing Date
3.1	Restated Certificate of Incorporation, as amended	Form 10-Q	3.1	August 9, 2016
3.2	Restated Bylaws	Form 8-K	3.1	February 17, 2016
4.1	Form of Common Stock Certificate	Form S-8(1)	4.3	November 7, 2012
4.2	Indenture, dated as of July 6, 2016, between the Registrant and U.S. Bank National Association, as trustee	Form 8-K	4.1	July 6, 2016
4.3	First Supplemental Indenture (including the Form of Note), dated as of July 6, 2016, between the Registrant and U.S. Bank National Association, as trustee	Form 8-K	4.2	July 6, 2016
4.4	Form of Senior Indenture	Form S-3(2)	4.1	May 10, 2017
4.5	Form of Subordinated Indenture	Form S-3(2)	4.2	May 10, 2017
4.6	Form of Senior Note	Form S-3(2)	4.3	May 10, 2017
4.7	Form of Subordinated Note	Form S-3(2)	4.4	May 10, 2017
4.8	Securities Purchase Agreement, dated April 4, 2018, between the Registrant and the purchasers named therein	Form 8-K	10.1	April 10, 2018
10.1#	Intercept Pharmaceuticals, Inc. 2012 Equity Incentive Plan	Form S-1/A(3)	10.2.1	September 27, 2012
10.2#	Form of Stock Option Grant Notice and Agreement for Directors	Form S-1/A(3)	10.2.2	September 27, 2012
10.3#	Form of Stock Option Grant Notice and Agreement for Employees and Consultants	Form S-1/A(3)	10.2.3	September 27, 2012

Exhibit Number	Exhibit Description	Incorporated herein by reference		
		Form†	Exhibit	Filing Date
10.4#	Form of Restricted Stock Unit Award Grant Notice and Agreement for Directors	Form S-1/A[3]	10.2.4	September 27, 2012
10.5#	Form of Restricted Stock Unit Award Grant Notice and Agreement for Employees and Consultants	Form S-1/A[3]	10.2.5	September 27, 2012
10.6#	Form of Restricted Stock Award Grant Notice and Agreement for Directors	Form 10-Q	10.3	May 9, 2014
10.7#	Form of Restricted Stock Award Grant Notice and Agreement for Employees and Consultants	Form 10-Q	10.4	May 9, 2014
10.8#	Form of Performance Stock Unit Grant Notice and Agreement	Form 10-Q	10.5	May 10, 2018
10.9#	Form of Performance Share Grant Notice and Agreement	Form 10-Q	10.6	May 10, 2018
10.10#	Amended and Restated Employment Agreement, effective May 14, 2013, between the Registrant and Mark Pruzanski	Form 10-Q	10.5	May 14, 2013
10.11#	Employment Agreement, effective May 3, 2016, between the Registrant and Sandip S. Kapadia	Form 10-Q	10.1.1	August 9, 2016
10.12#	Employment Agreement, effective February 15, 2017, between the Registrant and Jerome B. Durso	Form 10-Q	10.1	May 10, 2017
10.13#	Employment Agreement, effective April 14, 2017, between the Registrant and David Ford	Form 10-Q	10.1	August 3, 2017
10.14#	Amended and Restated Employment Agreement, effective as of November 27, 2017, between the Registrant and David Shapiro	Form 8-K	10.2	December 1, 2017
10.15#	Form of Indemnification Agreement for directors and executive officers of the Registrant	Form S-1[3]	10.7	September 4, 2012
10.16	Base Call Option Confirmation, dated June 30, 2016, between the Registrant and Royal Bank of Canada	Form 8-K	10.1	July 6, 2016
10.17	Base Call Option Confirmation, dated June 30, 2016, between the Registrant and UBS AG, London Branch	Form 8-K	10.3	July 6, 2016
10.18	Base Call Option Confirmation, dated June 30, 2016, between the Registrant and Credit Suisse Capital LLC	Form 8-K	10.5	July 6, 2016
10.19	Additional Call Option Confirmation, dated July 1, 2016, between the Registrant and Royal Bank of Canada	Form 8-K	10.2	July 6, 2016
10.20	Additional Call Option Confirmation, dated July 1, 2016, between the Registrant and UBS AG, London Branch	Form 8-K	10.4	July 6, 2016
10.21	Additional Call Option Confirmation, dated July 1, 2016, between the Registrant and Credit Suisse Capital LLC	Form 8-K	10.6	July 6, 2016
10.22	Lease Agreement between The Irvine Company LLC and the Registrant, dated May 1, 2014	Form 8-K	10.1	May 7, 2014
10.23	Second Amendment to Lease, dated as of July 19, 2016, between the Registrant and Irvine Eastgate Office II LLC	Form 10-Q	10.7	November 9, 2016

Exhibit Number	Exhibit Description	Incorporated herein by reference		
		Form†	Exhibit	Filing Date
10.24	Third Amendment to Lease, dated as of June 21, 2018, between the Registrant and Irvine Eastgate Office II LLC	Form 10-Q	10.1	August 7, 2018
10.25	Fourth Amendment to Lease, dated as of October 30, 2018, between the Registrant and Irvine Eastgate Office II LLC	Form 10-Q	10.1	November 1, 2018
10.26	Underlease between the Registrant, Intercept Pharma Europe Ltd. and Performing Right Society, Ltd., dated January 22, 2016	Form 10-K	10.12	February 29, 2016
10.27	Lease Agreement, dated December 7, 2016, between the Registrant and Legacy Yards Tenant LP	Form 10-K	10.17	March 1, 2017
10.28	First Amendment to Lease Agreement, dated June 27, 2017, between the Registrant and Legacy Yards Tenant LP	Form 10-Q	10.1	November 6, 2017
10.29	Second Amendment to Lease, dated June 22, 2018, between the Registrant and Legacy Yards Tenant LP	Form 10-Q	10.2	August 7, 2018
10.30	Termination of Lease, dated December 31, 2017, between the Registrant and One Hudson Yards Owner LLC	Form 10-K	10.21	February 28, 2018
10.31+	Commercial Manufacturing and Supply Agreement, dated August 12, 2016, between the Registrant and PharmaZell GMBH	Form 10-Q	10.8	November 9, 2016
10.32+	Amendment #1 to Manufacturing and Supply Agreement, dated December 12, 2017, between the Registrant and PharmaZell GMBH	Form 10-K	10.2.1	February 28, 2018
10.33+	Sumitomo Agreement, dated March 29, 2011, between the Registrant and Sumitomo Dainippon Pharma Co., Ltd.	Form S-1/A(3)	10.10	September 27, 2012
10.34	Amendment No. 1, dated June 8, 2011, to that certain Sumitomo Agreement, dated March 29, 2011, between the Registrant and Sumitomo Dainippon Pharma Co., Ltd.	Form 10-Q	10.1	May 10, 2018
10.35	Amendment No. 2, dated September 16, 2011, to that certain Sumitomo Agreement, dated March 29, 2011, between the Registrant and Sumitomo Dainippon Pharma Co., Ltd.	Form 10-Q	10.2	May 10, 2018
10.36+	Amendment No. 3, dated February 13, 2018, to that certain Sumitomo Agreement, dated March 29, 2011, between the Registrant and Sumitomo Dainippon Pharma Co., Ltd.	Form 10-Q	10.3	May 10, 2018
21.1*	Subsidiaries of the Registrant			
23.1*	Consent of Independent Registered Public Accounting Firm			
24.1*	Power of Attorney (included in signature page to this Annual Report on Form 10-K)			
31.1*	Certification of Principal Executive Officer required by Rule 13a-14(a) or Rule 15d-14(a)			
31.2*	Certification of Principal Financial Officer required by Rule 13a-14(a) or Rule 15d-14(a)			

Exhibit Number	Exhibit Description	Incorporated herein by reference		
		Form†	Exhibit	Filing Date
32*[4]	Certifications required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. 1350)			
101*	The following materials from the Registrant's Annual Report on Form 10-K for the year ended December 31, 2018, formatted in XBRL (eXtensible Business Reporting Language): (i) Consolidated Balance Sheets as of December 31, 2018 and 2017, (ii) Consolidated Statements of Operations for the Years Ended December 31, 2018, 2017 and 2016, (iii) Consolidated Statements of Comprehensive Loss for the Years Ended December 31, 2018, 2017 and 2016, (iv) Consolidated Statements of Changes in Stockholders' Equity for the Years Ended December 31, 2018, 2017 and 2016, (v) Consolidated Statements of Cash Flows for the Years Ended December 31, 2018, 2017 and 2016 and (vi) Notes to Consolidated Financial Statements			

* Filed herewith.

\+ Confidential treatment has been received with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission (''SEC'').

\# Indicates a management contract or compensatory plan or arrangement.

† Unless otherwise specified, the File No. is 001-35668.

(1) Registration Statement on Form S-8 filed by the Registrant, Registration No. 333-184810.

(2) Registration Statement on Form S-1 filed by the Registrant, Registration No. 333-217861.

(3) Registration Statement on Form S-1 filed by the Registrant, Registration No. 333-183706.

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

Item 16. Form 10-K Summary

None.

SIGNATURES

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

INTERCEPT PHARMACEUTICALS, INC.

Date: March 1, 2019

By: /s/ Mark Pruzanski, M.D.
Mark Pruzanski, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: March 1, 2019

By: /s/ Sandip Kapadia
Sandip Kapadia
Chief Financial Officer and Treasurer
(Principal Financial Officer and Principal Accounting Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Mark Pruzanski, M.D. and Sandip Kapadia, and each of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her, and in his or her name, place and 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 all other documents in connection therewith, with the Securities and Exchange Commission, granting unto each said attorney-in-fact and agent full power and authority to do and perform each and every act and thing required or necessary to be done in and about the premises, as fully and to all intents and purposes as the undersigned could do in person, and hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them 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, this report has been signed below by the following persons on behalf of the registrant and in the capacities indicated on March 1, 2019.

Signature	Title
/s/ Mark Pruzanski, M.D. Mark Pruzanski, M.D.	President, Chief Executive Officer and Director (Principal Executive Officer)
/s/ Sandip Kapadia Sandip Kapadia	Chief Financial Officer and Treasurer (Principal Financial Officer and Principal Accounting Officer)
/s/ Paolo Fundarò Paolo Fundarò	Chairman of the Board of Directors
/s/ Srinivas Akkaraju, M.D., Ph.D. Srinivas Akkaraju, M.D., Ph.D.	Director
/s/ Luca Benatti, Ph.D. Luca Benatti, Ph.D.	Director
/s/ Daniel Bradbury Daniel Bradbury	Director
/s/ Keith Gottesdiener, M.D. Keith Gottesdiener, M.D.	Director
/s/ Nancy Miller-Rich Nancy Miller-Rich	Director

Signature	Title
/s/ Gino Santini Gino Santini	Director
/s/ Glenn Sblendorio Glenn Sblendorio	Director
/s/ Daniel Welch Daniel Welch	Director

[This page intentionally left blank.]

INTERCEPT PHARMACEUTICALS, INC.

Index to Consolidated Financial Statements

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and Board of Directors
Intercept Pharmaceuticals, Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Intercept Pharmaceuticals, Inc. and subsidiaries (the Company) as of December 31, 2018 and 2017, the related consolidated statements of operations, comprehensive loss, changes in stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2018, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission, and our report dated March 1, 2019 expressed an unqualified opinion on the effectiveness of the Company's internal control over financial reporting.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ KPMG LLP

We have served as the Company's auditor since 2008.

New York, New York
March 1, 2019

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and Board of Directors
Intercept Pharmaceuticals, Inc.:

Opinion on Internal Control Over Financial Reporting

We have audited Intercept Pharmaceuticals, Inc.'s and subsidiaries (the Company) internal control over financial reporting as of December 31, 2018, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission. In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2018 and 2017, the related consolidated statements of operations, comprehensive loss, changes in stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2018, and the related notes (collectively, the ''consolidated financial statements''), and our report dated March 1, 2019 expressed an unqualified opinion on those consolidated financial statements.

Basis for Opinion

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

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

Definition and Limitations of Internal Control Over Financial Reporting

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

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

/s/ KPMG LLP

New York, New York
March 1, 2019

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Balance Sheets

	December 31, 2018	December 31, 2017
	(in thousands, except share and per share data)	
Assets		
Current assets:		
Cash and cash equivalents	$ 43,248	$ 70,013
Investment debt securities, available-for-sale	392,912	344,904
Accounts receivable, net	25,694	16,501
Prepaid expenses and other current assets	20,571	16,889
Total current assets	482,425	448,307
Fixed assets, net	10,411	16,184
Inventory, net	7,108	3,480
Security deposits	9,223	16,376
Total assets	$ 509,167	$ 484,347
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable, accrued expenses and other liabilities	$ 105,109	$ 94,777
Short-term interest payable	7,475	7,475
Short-term portion of deferred revenue	1,621	1,782
Total current liabilities	114,205	104,034
Long-term liabilities:		
Long-term debt	371,250	355,677
Long-term other liabilities	3,771	5,578
Long-term portion of deferred revenue	811	2,672
Total liabilities	$ 490,037	$ 467,961
Commitments and contingencies (Note 15)		
Stockholders' equity:		
Common stock par value $0.001 per share; 45,000,000 shares authorized; 29,693,876 and 25,172,678 shares issued and outstanding as of December 31, 2018 and December 31, 2017, respectively	30	25
Additional paid-in capital	1,800,144	1,486,690
Accumulated other comprehensive loss, net	(2,259)	(786)
Accumulated deficit	(1,778,785)	(1,469,543)
Total stockholders' equity	19,130	16,386
Total liabilities and stockholders' equity	$ 509,167	$ 484,347

See accompanying notes to consolidated financial statements.

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Statements of Operations

	Years Ended December 31,		
	2018	2017	2016
	(in thousands, except per share data)		
Revenue:			
Product revenue, net	$ 177,782	$ 129,175	$ 18,169
Licensing revenue	2,022	1,781	6,782
Total revenue	179,804	130,956	24,951
Operating expenses:			
Cost of sales	2,519	1,371	—
Selling, general and administrative	255,474	273,698	273,596
Research and development	207,301	191,499	153,893
Total operating expenses	465,294	466,568	427,489
Operating loss	(285,490)	(335,612)	(402,538)
Other income (expense):			
Interest expense	(30,523)	(29,271)	(14,196)
Other income, net	6,771	4,516	3,904
	(23,752)	(24,755)	(10,292)
Net loss	$(309,242)	$(360,367)	$(412,830)
Net loss per common and potential common share:			
Basic and diluted	$ (10.86)	$ (14.38)	$ (16.74)
Weighted average common and potential common shares outstanding:			
Basic and diluted	28,464	25,054	24,663

See accompanying notes to consolidated financial statements.

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Statements of Comprehensive Loss

	Years Ended December 31,		
	2018	2017	2016
		(in thousands)	
Net loss	$(309,242)	$(360,367)	$(412,830)
Other comprehensive (loss) income:			
Net changes related to available-for-sale investment debt securities:			
Unrealized gains on investment debt securities	88	791	378
Reclassification adjustment for realized losses on investment debt securities included in other income, net	(8)	—	(48)
Net unrealized gains on investment debt securities	$ 80	$ 791	$ 330
Foreign currency translation gains (losses)	(1,553)	1,225	(878)
Comprehensive loss	$(310,715)	$(358,351)	$(413,378)

See accompanying notes to consolidated financial statements.

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Statements of Changes in Stockholders' Equity
For the Years Ended December 31, 2018, 2017 and 2016
(in thousands)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Stockholders' Equity
	Shares	Amount				
Balance – December 31, 2015	24,392	$24	$1,300,008	$ (695,630)	$(2,253)	$ 602,149
Stock-based compensation	—	—	46,205	—	—	46,205
Recognition of debt discount on Convertible Notes	—	—	113,145	—	—	113,145
Purchase of Capped Call Transactions and associated costs	—	—	(38,364)	—	—	(38,364)
Net proceeds from exercise of stock options	428	1	5,174	—	—	5,175
Other comprehensive loss	—	—	—	—	(548)	(548)
Net loss	—	—	—	(412,830)	—	(412,830)
Balance – December 31, 2016	24,820	$25	$1,426,168	$(1,108,460)	$(2,801)	$ 314,932
Stock-based compensation	—	—	56,968	—	—	56,968
Net proceeds from exercise of stock options	353	—	2,838	—	—	2,838
Other comprehensive income	—	—	716	(716)	2,015	2,015
Net loss	—	—	—	(360,367)	—	(360,367)
Balance – December 31, 2017	25,173	$25	$1,486,690	$(1,469,543)	$ (786)	$ 16,386
Stock-based compensation	—	—	49,914	—	—	49,914
Issuance of common stock from public and private placement offerings, net of underwriting fees and issuance costs	4,258	5	261,357	—	—	261,362
Net proceeds from exercise of stock options	263	—	4,363	—	—	4,363
Employee withholding taxes related to stock-based awards		—	(2,180)			(2,180)
Other comprehensive loss	—	—	—	—	(1,473)	(1,473)
Net loss	—	—	—	(309,242)	—	(309,242)
Balance – December 31, 2018	29,694	$30	$1,800,144	$(1,778,785)	$(2,259)	$ 19,130

See accompanying notes to consolidated financial statements.

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Statements of Cash Flows

	Years Ended December 31,		
	2018	2017	2016
		(in thousands)	
Cash flows from operating activities:			
Net loss	$(309,242)	$(360,367)	$(412,830)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	49,914	56,968	46,205
(Accretion) amortization of (discount) premium on investment debt securities	(33)	3,429	4,939
Amortization of deferred financing costs	1,542	1,417	685
Realized loss on investments	8	—	48
Depreciation	4,582	4,601	3,831
Loss on the disposal of fixed assets	1,331	1,000	—
Accretion of debt discount	14,031	12,904	6,242
Changes in operating assets:			
Prepaid expenses and other current assets	(3,682)	(7,535)	4,284
Security deposits	7,153	1,438	(13,796)
Accounts receivable	(9,193)	(7,375)	(9,126)
Inventory	(3,628)	(1,201)	(2,279)
Changes in operating liabilities:			
Accounts payable, accrued expenses and other current liabilities	10,332	29,226	19,960
Interest payable	—	208	7,267
Long-term other liabilities	(1,807)	5,578	—
Deferred revenue	(2,022)	(5,693)	2,129
Net cash used in operating activities	(240,714)	(265,402)	(342,441)
Cash flows from investing activities:			
Purchases of investment debt securities	(436,071)	(231,107)	(511,521)
Sales and maturities of investment debt securities	388,168	529,274	456,465
Purchases of equipment, leasehold improvements, and furniture and fixtures	(167)	(10,392)	(5,079)
Net cash (used in) provided by investing activities	(48,070)	287,775	(60,135)
Cash flows from financing activities:			
Proceeds from issuance of common stock, net of issuance costs	261,362	—	—
Payments for Capped Call Transactions and associated costs	—	—	(38,364)
Proceeds from issuance of Convertible Notes, net of issuance costs	—	—	447,573
Proceeds from exercise of options, net	4,363	2,838	5,173
Payments of employee withholding taxes related to stock-based awards	(2,180)	—	—
Net cash provided by financing activities	263,545	2,838	414,382
Effect of exchange rate changes	(1,526)	1,127	(873)
Net (decrease) increase in cash and cash equivalents	(26,765)	26,338	10,933
Cash and cash equivalents – beginning of period	70,013	43,675	32,742
Cash and cash equivalents – end of period	$ 43,248	$ 70,013	$ 43,675

See accompanying notes to consolidated financial statements.

1. Overview of Business

Intercept Pharmaceuticals, Inc. (the ''Company'') is a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat progressive non-viral liver diseases, including primary biliary cholangitis (''PBC'') and nonalcoholic steatohepatitis (''NASH''). The Company currently has one marketed product, Ocaliva (obeticholic acid or ''OCA''). Founded in 2002 in New York, the Company has operations in the United States, Europe and Canada.

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The Company's financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (''U.S. GAAP''). The consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation. The Company has no unconsolidated subsidiaries or investments accounted for under the equity method.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and judgments that affect the reported amounts of assets and liabilities, the disclosure of assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from these estimates.

Foreign Currency

The Company's functional and reporting currency is the U.S. dollar. Transactions in foreign currencies are recorded at the exchange rate prevailing on the date of the transaction. The resulting monetary assets and liabilities are translated into U.S. dollars at exchange rates prevailing on the subsequent balance sheet date. Gains and losses as a result of translation adjustments are recorded within Other income, net in the accompanying consolidated statements of operations and within Foreign currency translation gains (losses) within the accompanying consolidated statements of comprehensive loss.

Cash and Cash Equivalents

The Company considers all highly liquid securities with an original or remaining maturity of three months or less at acquisition to be cash equivalents.

Investment Debt Securities, Available-for-Sale

Investment debt securities are considered to be available-for-sale and are carried at fair value. Unrealized gains and losses, if any, are reported in other comprehensive income (loss). The cost of investment debt securities classified as available-for-sale is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion is included in other income, net. Realized gains and losses, and declines in value judged to be other-than-temporary, if any, are also included in other income, net. The cost of securities sold is based on the specific identification method. The estimated fair value of the available-for-sale debt securities is determined based on quoted market prices or rates for similar instruments.

Fair Value of Financial Instruments

Financial instruments, including cash and cash equivalents, receivables, accounts payable and accrued liabilities are carried at cost which management believes approximates fair value because of the short-term maturity of these instruments.

Risks and Uncertainties

The Company is subject to risks common to companies in the pharmaceutical industry including failing to secure additional funding and uncertainties related to commercialization of products and regulatory approval.

2. Summary of Significant Accounting Policies – (continued)

Concentration of Credit Risk

Financial instruments, which potentially subject the Company to concentrations of credit risk, principally consist of cash, cash equivalents and investment debt securities. The Company currently invests its excess cash primarily in money market funds, U.S. Treasury notes, and high quality, marketable debt instruments of corporations, financial institutions and government sponsored enterprises. The Company has adopted an investment policy that includes guidelines relative to credit quality, diversification and maturities to preserve principal and liquidity. On a consolidated basis, for the year ended December 31, 2018, the Company's three largest customers (as discussed in more detail below under ''Revenue Recognition'') accounted for 38%, 28% and 16%, of the Company's net product sales, respectively. On a consolidated basis, for the year ended December 31, 2017, the Company's three largest customers (as discussed in more detail below under ''Revenue Recognition'') accounted for 40%, 23% and 13%, of the Company's net product sales, respectively.

Accounts Receivable

The Company extends credit to customers based on its evaluation of the customer's financial condition. The Company records receivables for all billings when amounts are due under standard terms. Accounts receivable are stated at amounts due net of applicable prompt pay discounts and other contractual adjustments as well as an allowance for doubtful accounts. The Company assesses the need for an allowance for doubtful accounts by considering a number of factors, including the length of time trade accounts receivable are past due, the customer's ability to pay its obligation and the condition of the general economy and the industry as a whole. The Company will write off accounts receivable when the Company determines that they are uncollectible. The Company has recorded $25.7 million and $16.5 million of accounts receivable as of December 31, 2018 and 2017, respectively, and has not recorded an allowance for any doubtful accounts as of December 31, 2018 and 2017. On a consolidated basis, the Company's three largest customers accounted for 22%, 29% and 6% of the December 31, 2018 accounts receivable balance, respectively. On a consolidated basis, the Company's three largest customers accounted for 34%, 29% and 12% of the December 31, 2017 accounts receivable balance, respectively.

Fixed Assets

Fixed assets are stated at cost, and depreciated over the estimated useful life of the assets. Depreciation is recorded using the straight-line method over the estimated useful lives of the respective assets, generally three to seven years. Leasehold improvements are amortized over the shorter of the asset's useful life or the life of the lease term. Expenditures for maintenance and repairs are charged to expense as incurred.

Impairment of Long-Lived Assets

Long-lived assets consist of fixed assets. The Company evaluates long-lived assets for impairment when events and circumstances indicate that the carrying amount of an asset or group of assets may not be fully recoverable. If indicators of impairment exist, the Company assesses the recoverability of the affected long-lived assets by determining whether the carrying value of such assets can be recovered through undiscounted future operating cash flows. If the carrying amount is not recoverable, the Company measures the amount of any impairment by comparing the carrying value of the asset to the present value of the expected future cash flows associated with the use of the asset.

Inventory

Inventories are stated at the lower of cost or estimated realizable value. The Company determines the cost of inventory using the first-in, first-out (or FIFO) method. The Company capitalizes inventory costs associated with the Company's product after regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized; otherwise, such costs are expensed as research and development. The Company periodically analyzes its

2. Summary of Significant Accounting Policies – (continued)

inventory levels to identify inventory that may expire prior to expected sale or has a cost basis in excess of its estimated realizable value, and writes-down such inventories as appropriate. In addition, the Company's product is subject to strict quality control and monitoring which the Company performs throughout the manufacturing process. If certain batches or units of product no longer meet quality specifications or become obsolete due to expiration, the Company records a charge to cost of sales sold to write down such unmarketable inventory to zero. No such charges were recorded in the years ended December 31, 2018, 2017 or 2016.

Convertible Senior Notes

The Company's 3.25% Convertible Senior Notes due 2023 (the "Convertible Notes") are accounted for in accordance with Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") Subtopic 470-20, *Debt with Conversion and Other Options*. ASC Subtopic 470-20 requires the issuer of convertible debt that may be settled in shares or cash upon conversion at the issuer's option, such as the Convertible Notes, to account for the liability (debt) and equity (conversion option) components separately. The value assigned to the debt component is the estimated fair value, as of the issuance date, of a similar debt instrument without the conversion option. The amount of the equity component (and resulting debt discount) is calculated by deducting the fair value of the liability component from the principal amount of the convertible debt instrument. The resulting debt discount is amortized as additional non-cash interest expense over the expected life of the notes utilizing the effective interest method. Although ASC 470-20 has no impact on the Company's actual past or future cash flows, it requires the Company to record non-cash interest expense as the debt discount is amortized. For additional information, see Note 8 — Long-Term Debt.

Revenue Recognition

Product Revenue, Net

The Company commenced its commercial launch of Ocaliva for the treatment of PBC in the United States in June 2016. In December 2016, the European Commission granted conditional approval for Ocaliva for the treatment of PBC and the Company commenced its European commercial launch in January 2017. Since January 2017, Ocaliva has also received regulatory approval in several of the Company's target markets outside the United States and Europe, including Canada, Israel and Australia. The Company sells Ocaliva to a limited number of specialty pharmacies which dispense the product directly to patients. The specialty pharmacies are referred to as the Company's customers.

The Company provides the right of return to its customers for unopened product for a limited time before and after its expiration date. Prior to July 2017, given the Company's limited sales history for Ocaliva and the inherent uncertainties in estimating product returns, the Company determined that the shipments of Ocaliva made to its customers did not meet the criteria for revenue recognition at the time of shipment. Accordingly, the Company recognized revenue when the product was sold through by its customers, provided all other revenue recognition criteria were met. The Company invoiced its customers upon shipment of Ocaliva to them and recorded accounts receivable, with a corresponding liability for deferred revenue equal to the gross invoice price. The Company then recognized revenue when Ocaliva was sold through as specialty pharmacies dispensed product directly to the patients (sell-through basis).

The Company re-evaluated its revenue recognition policy in the third quarter of 2017, which included the accumulation and review of customer-related transactions since the Company's commercial launch in the second quarter of 2016. The Company concluded it had accumulated sufficient data to reasonably estimate product returns and, therefore, began to recognize revenue at the time of shipment to its customers (sell-in basis). During the third quarter of 2017, the Company recorded an adjustment related to this change in estimate to recognize previously deferred revenue. The net effect was an increase in net sales of Ocaliva of $4.1 million for the year ended December 31, 2017. The Company also established a new reserve of $0.7 million during 2017 related to future returns from its customers.

2. Summary of Significant Accounting Policies – (continued)

Effective January 1, 2018, the Company began recognizing revenue under ASC Topic 606, *Revenue from Contracts with Customers* (''ASC 606''). The core principle of this revenue standard is that a company should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the company expects to be entitled in exchange for those goods or services. The following five steps are applied to achieve that core principle:

- Step 1: Identify the contract with the customer
- Step 2: Identify the performance obligations in the contract
- Step 3: Determine the transaction price
- Step 4: Allocate the transaction price to the performance obligations in the contract
- Step 5: Recognize revenue when the company satisfies a performance obligation

In order to identify the performance obligations in a contract with a customer, a company must assess the promised goods or services in the contract and identify each promised good or service that is distinct. A performance obligation meets ASC 606's definition of a ''distinct'' good or service (or bundle of goods or services) if both of the following criteria are met:

- The customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (i.e., the good or service is capable of being distinct).
- The entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract (i.e., the promise to transfer the good or service is distinct within the context of the contract).

If a good or service is not distinct, the good or service is combined with other promised goods or services until a bundle of goods or services is identified that is distinct.

The transaction price is the amount of consideration to which an entity expects to be entitled in exchange for transferring promised goods or services to a customer, excluding amounts collected on behalf of third parties (for example, some sales taxes). The consideration promised in a contract with a customer may include fixed amounts, variable amounts, or both. Variable consideration is included in the transaction price only to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved.

The transaction price is allocated to each performance obligation on a relative standalone selling price basis. The transaction price allocated to each performance obligation is recognized when that performance obligation is satisfied, at a point in time or over time as appropriate.

Under ASC 606, the Company has written contracts with each of its customers that have a single performance obligation — to deliver products upon receipt of a customer order — and these obligations are satisfied when delivery occurs and the customer receives Ocaliva. The Company evaluates the creditworthiness of each of its customers to determine whether collection is reasonably assured. The Company estimates variable revenue by calculating gross product revenues based on the wholesale acquisition cost that the Company charges its customers for Ocaliva, and then estimating its net product revenues by deducting (i) trade allowances, such as invoice discounts for prompt payment and customer fees, (ii) estimated government rebates and discounts related to Medicare, Medicaid and other government programs, and (iii) estimated costs of incentives offered to certain indirect customers including patients.

2. Summary of Significant Accounting Policies – (continued)

Trade Allowances

The Company provides invoice discounts on Ocaliva sales to certain of its customers for prompt payment and records these discounts as a reduction to gross product revenues. These discounts are based on contractual terms.

Rebates and Discounts

The Company contracts with the Centers for Medicare & Medicaid Services and other government agencies to make Ocaliva available to eligible patients. As a result, the Company estimates any rebates and discounts and deducts these estimated amounts from its gross product revenues at the time the revenues are recognized. The Company's estimates of rebates and discounts are based on the government mandated discounts, which are statutorily-defined and applicable to these government funded programs. These estimates are recorded in accounts payable, accrued expenses and other liabilities on the consolidated balance sheet.

Other Incentives

Other incentives that the Company offers to indirect customers include co-pay assistance cards provided by the Company for PBC patients who reside in states that permit co-pay assistance programs. The Company's co-pay assistance program is intended to reduce each participating patient's portion of the financial responsibility for Ocaliva purchase price to a specified dollar amount. The Company estimates the amount of co-pay assistance provided to eligible patients based on the terms of the program when product is dispensed by the specialty pharmacies to the patients. These estimates are based on redemption information provided by third-party claims processing organizations and are recorded in accounts payable, accrued expenses and other liabilities on the consolidated balance sheet.

Because the Company changed its revenue recognition polices to the sell-in basis during the year ended December 31, 2017, the adoption of ASU 2014-09 (as defined below), via a modified retrospective approach applied to all contracts not completed at January 1, 2018, did not result in an adjustment to amounts previously recognized as revenue under ASC Topic 605, *Revenue Recognition* (''ASC 605''), and there were no other significant changes impacting the timing or measurement of the Company's revenue or the Company's business processes and controls.

Licensing Revenue

Under ASC 606, the Company accounts for the development, regulatory and sales milestones within an arrangement as variable consideration that is included in the transaction price only to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. Because the achievement of the milestones triggering these payments is highly susceptible to factors outside the entity's influence, and the uncertainty about the amount of consideration for some of the milestones is not expected to be resolved for a long period of time, the Company does not expect to record the associated revenue until achievement of each milestone is imminent or has already occurred. Adoption of ASC 606 did not result in any adjustment to licensing revenue previously recognized under ASC 605.

Research and Development Expenses

Research and development costs that do not have alternative future use are charged to expense as incurred. This includes the cost of conducting clinical trials, compensation and related overhead for employees and consultants involved in research and development and the cost of the Company's manufacturing activities to supply ongoing and future clinical trials and preclinical studies as well as preparations for commercialization of OCA. The cost of a compound that is acquired prior to regulatory approval, does not constitute a business and has no alternative future use is charged to expense as incurred. For periods prior to the commercial launch of Ocaliva for PBC in June 2016, all manufacturing costs for OCA were expensed as research and development expenses. The Company will continue to incur manufacturing costs for OCA for other indications such as NASH prior to their approval.

2. Summary of Significant Accounting Policies – (continued)

Stock-based Compensation

The Company accounts for stock-based compensation in accordance with ASC Topic 718, *Compensation — Stock Compensation* (''ASC 718''). The Company estimates the fair value of stock option awards using the Black-Scholes option pricing model on the date of the grant. Restricted stock unit awards (''RSUs'') and restricted stock awards (''RSAs'') without a market condition are valued based on the closing price of the Company's common stock on the date of the grant. The fair value of time-based equity awards is recognized and amortized on a straight-line basis over the requisite service period of the award. Stock options granted to employees generally fully vest over four years and have a term of ten years. The Company recognizes stock-based compensation expense for options and other stock-based awards with performance conditions ratably over the performance period once the pre-defined performance-based criteria for vesting becomes probable. The fair value of awards with market conditions is estimated using the Monte Carlo simulation method and expense is recognized on a straight-line basis over the requisite service period of the award. The Company recognizes stock-based compensation for non-employees (other than non-employee directors) on a mark-to-market basis, which is updated on a quarterly basis.

Net Income (Loss) Per Share

Basic net income (loss) per share is computed by dividing net income (loss) attributable to common stockholders (numerator) by the weighted average number of common shares outstanding (denominator) during the period. Diluted net income (loss) per share gives effect to all dilutive potential common shares outstanding during the period, including the Convertible Notes, stock options and RSUs, as applicable, using the treasury stock method.

Income Taxes

The Company utilizes the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial statement carrying amounts and tax bases of assets and liabilities using enacted tax rates in effect for years in which the temporary differences are expected to reverse. The Company establishes a valuation allowance when it believes it is more likely than not that deferred tax assets will not be realized.

The Company determines the need for a valuation allowance by assessing the probability of realizing deferred tax assets, taking into consideration all available positive and negative evidence, including historical operating results, expectations of future taxable income, carryforward periods available, various income tax strategies and other relevant factors. Significant judgment is required in making this assessment and to the extent future expectations change, the Company would have to assess the recoverability of its deferred assets at that time. At December 31, 2018 and 2017, the Company maintained a full valuation allowance on its deferred tax assets.

At any one time the Company's tax returns for numerous tax years are subject to examination by U.S. Federal, state, and foreign taxing jurisdictions. The impact of an uncertain tax position taken or expected to be taken on an income tax return must be recognized in the financial statements at the largest amount that is more likely than not to be sustained. An uncertain income tax position will not be recognized in the financial statements unless it is more likely than not to be sustained. At December 31, 2018 and 2017, the Company had no reserves for unrecognized tax benefits.

Segments

The Company operates in one segment. The Company is a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat progressive non-viral liver diseases.

Recent Accounting Pronouncements

In May 2014, the FASB issued Accounting Standards Update (''ASU'') No. 2014-09, ''Revenue from Contracts with Customers (Topic 606)'' (''ASU 2014-09''), and subsequently issued modifications or

2. Summary of Significant Accounting Policies – (continued)

clarifications in ASU No. 2015-14, ''Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date,'' ASU No. 2016-08, ''Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations (Reporting Revenue Gross versus Net),'' ASU No. 2016-10, ''Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing'' and ASU No. 2016-12, ''Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients.'' The revenue recognition principle in ASU 2014-09 and the related guidance is that an entity should recognize revenue to depict the transfer of goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. ASU 2014-09 prescribes a five-step process for evaluating contracts and determining revenue recognition. In addition, new and enhanced disclosures are required. Companies may adopt the new standard using either the full retrospective approach, a modified retrospective approach with practical expedients, or a cumulative effect upon adoption approach. The Company adopted the new standard on January 1, 2018, using the modified retrospective approach, applied only to contracts that were not completed as of January 1, 2018. The adoption did not have an impact on the Company's consolidated financial statements and related disclosures.

In January 2016, the FASB issued ASU No. 2016-01, ''Financial Instruments-Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities'' (''ASU 2016-01''). ASU 2016-01 requires equity investments to be measured at fair value with changes in fair value recognized in net income; simplifies the impairment assessment of equity investments without readily determinable fair values by requiring a qualitative assessment to identify impairment; eliminates the requirement for public business entities to disclose the method(s) and significant assumptions used to estimate the fair value that is required to be disclosed for financial instruments measured at amortized cost on the balance sheet; requires public business entities to use the exit price notion when measuring the fair value of financial instruments for disclosure purposes; requires an entity to present separately in other comprehensive income the portion of the total change in the fair value of a liability resulting from a change in the instrument-specific credit risk when the entity has elected to measure the liability at fair value in accordance with the fair value option for financial instruments; requires separate presentation of financial assets and financial liabilities by measurement category and form of financial assets on the balance sheet or the accompanying notes to the financial statements and clarifies that an entity should evaluate the need for a valuation allowance on a deferred tax asset related to available-for-sale securities in combination with the entity's other deferred tax assets. ASU 2016-01 is effective for financial statements issued for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. The Company adopted ASU 2016-01 on January 1, 2018 and its adoption did not have a material impact on the Company's consolidated financial statements and related disclosures.

In February 2016, the FASB established ASC Topic 842, *Leases* (''ASC 842''), by issuing ASU No. 2016-02, which requires lessees to recognize leases on-balance sheet and disclose key information about leasing arrangements. ASC 842 was subsequently amended by ASU No. 2018-01, ''Land Easement Practical Expedient for Transition to Topic 842''; ASU No. 2018-10, ''Codification Improvements to Topic 842, Leases''; and ASU No. 2018-11, ''Targeted Improvements''. The new standard establishes a right-of-use model (''ROU'') that requires a lessee to recognize a ROU asset and lease liability on the balance sheet for all leases with a term longer than 12 months. Leases will be classified as finance or operating, with classification affecting the pattern and classification of expense recognition in the income statement. A modified retrospective transition approach is required, applying the new standard to all leases existing at the date of initial application. An entity may choose to use either (1) its effective date or (2) the beginning of the earliest comparative period presented in the financial statements as its date of initial application. The Company adopted the new standard on January 1, 2019 using the effective date as the date of initial application. Consequently, financial information will not be updated and the disclosures required under the new standard will not be provided for dates and periods before January 1, 2019. The new standard provides a number of optional practical expedients in transition. The Company elected the ''package of practical expedients'', which

2. Summary of Significant Accounting Policies – (continued)

permits the Company to not reassess under the new standard the Company's prior conclusions about lease identification, lease classification and initial direct costs. The new standard also provides practical expedients for an entity's ongoing accounting. The Company elected the short-term lease recognition exemption for all leases that qualify. This means, for those leases that qualify, the Company will not recognize ROU assets or lease liabilities, and this includes not recognizing ROU assets or lease liabilities for existing short-term leases of those assets in transition. The Company also elected the practical expedient to not separate lease and non-lease components for all of the Company's leases. Upon adoption, the Company will recognize additional operating liabilities of $25.4 million, with corresponding ROU assets of $19.6 million based on the present value of the remaining minimum rental payments under current leasing standards for existing operating leases.

In May 2017, the FASB issued ASU No. 2017-09, ''Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting'' (''ASU 2017-09''), which clarifies when to account for a change to the terms or conditions of a stock-based payment award as a modification. Under the new guidance, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions. It is effective prospectively for the annual period ending December 31, 2018 and interim periods within that annual period. Early adoption is permitted. The Company adopted ASU 2017-09 on January 1, 2018 and its adoption did not have a material impact on the Company's consolidated financial statements and related disclosures.

In July 2017, the FASB issued ASU No. 2017-11, ''Earnings Per Share (Topic 260), Distinguishing Liabilities from Equity (Topic 480) and Derivatives and Hedging (Topic 815): I. Accounting for Certain Financial Instruments with Down Round Features; II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception'' (''ASU 2017-11''). Part I of this update addresses the complexity of accounting for certain financial instruments with down round features. Down round features are features of certain equity-linked instruments (or embedded features) that result in the strike price being reduced on the basis of the pricing of future equity offerings. Current accounting guidance creates cost and complexity for entities that issue financial instruments (such as warrants and convertible instruments) with down round features that require fair value measurement of the entire instrument or conversion option. Part II of this update addresses the difficulty of navigating ASC Topic 480, *Distinguishing Liabilities from Equity*, because of the existence of extensive pending content in the FASB Accounting Standards Codification. This pending content is the result of the indefinite deferral of accounting requirements about mandatorily redeemable financial instruments of certain nonpublic entities and certain mandatorily redeemable noncontrolling interests. The amendments in Part II of this update do not have an accounting effect. This ASU is effective for fiscal years, and interim periods within those years, beginning after December 15, 2018. The Company adopted ASU 2017-11 on January 1, 2019 and its adoption did not have any impact on the Company's consolidated financial statements and related disclosures.

In June 2018, the FASB issued ASU No. 2018-07, ''Improvements to Nonemployee Share-Based Payment Accounting'' (''ASU 2018-07''), which simplifies the accounting for share-based payments granted to nonemployees for goods and services. Under this ASU, most of the guidance on such payments to nonemployees would be aligned with the requirements for share-based payments granted to employees. The changes take effect for public companies for fiscal years starting after December 15, 2018, including interim periods within that fiscal year. For all other entities, the amendments are effective for fiscal years beginning after December 15, 2019, and interim periods within fiscal years beginning after December 15, 2020. Early adoption is permitted, but no earlier than an entity's adoption date of ASC 606. The Company adopted ASU 2018-07 on January 1, 2019 and its adoption did not have a material impact on the Company's consolidated financial statements and related disclosures.

In August 2018, the FASB issued ASU No. 2018-13, ''Fair Value Measurement (Topic 820): Disclosure Framework — Changes to the Disclosure Requirements for Fair Value Measurement'' (''ASU 2018-13''),

2. Summary of Significant Accounting Policies – (continued)

which makes a number of changes meant to add, modify or remove certain disclosure requirements associated with the movement amongst or hierarchy associated with Level 1, Level 2 and Level 3 fair value measurements. This guidance is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. Early adoption is permitted upon issuance of the update. The Company plans to adopt ASU 2018-13 effective January 1, 2020 and does not expect the adoption of this guidance to have a material impact on the Company's consolidated financial statements and related disclosures.

3. Significant Agreements

Sumitomo Dainippon Pharma Co., Ltd.

In March 2011, the Company entered into an exclusive license agreement (the ''Original Sumitomo Agreement'') with Sumitomo Dainippon Pharma Co., Ltd. (''Sumitomo Dainippon''), pursuant to which the Company granted to Sumitomo Dainippon an exclusive license to research, develop and commercialize OCA for the treatment of PBC and NASH in Japan and China (excluding Taiwan) and an option to research, develop and commercialize OCA in certain countries outside of such territories (the ''Country Option''). The Company received an upfront payment from Sumitomo Dainippon of $15.0 million under the terms of the Original Sumitomo Agreement. In May 2014, Sumitomo Dainippon exercised the Country Option in part to add Korea as part of its licensed territories and paid the Company a $1.0 million upfront fee in connection therewith. In February 2018, the Company and Sumitomo Dainippon entered into Amendment No. 3 (the ''Sumitomo Amendment'') to the Original Sumitomo Agreement (as amended, the ''Sumitomo Agreement''). Pursuant to the Sumitomo Amendment, (i) Sumitomo Dainippon agreed to return the rights to develop and commercialize OCA in Japan and Korea and waived its rights to the Country Option, (ii) the Company agreed to forego any further milestone or royalty payments relating to the development and commercialization of OCA in Japan and Korea and (iii) certain milestone payment obligations with respect to the development and commercialization of OCA were adjusted. In addition, the Company and Sumitomo Dainippon agreed that if certain clinical development milestones in China are not met by December 31, 2020, Sumitomo Dainippon may choose either to make a milestone payment to the Company or terminate the Sumitomo Agreement. Sumitomo Dainippon may also terminate the Sumitomo Agreement in its entirety or on an indication-by-indication basis at any time upon 90 days' written notice. As of December 31, 2018, the Company had achieved $6.0 million of development milestones under the Sumitomo Agreement. The Company may be eligible to receive additional milestone payments under the Sumitomo Agreement in an aggregate amount of up to approximately $23.0 million based on the occurrence of certain clinical trial and regulatory-related events and tiered royalty payments up to the mid-twenties in percentage terms based on net sales of OCA products in China (excluding Taiwan). Sumitomo Dainippon is responsible for the costs of developing and commercializing OCA in its territory.

The Company has concluded that Sumitomo Dainippon does not represent a customer of the Company, and therefore the Sumitomo Agreement is outside of the scope of ASC 606. The Company has accounted, and continues to account, for this agreement under the legacy accounting guidance. Under ASC 605, the Company evaluated this agreement and determined that it is a revenue arrangement with multiple deliverables, or performance obligations. The Company's substantive performance obligations under this agreement include an exclusive license to its technology, technical and scientific support to the development plan and participation on a joint steering committee. The Company determined that these performance obligations represent a single unit of accounting, since, initially, the license does not have stand-alone value to Sumitomo Dainippon without the Company's technical expertise and steering committee participation during the development of OCA. The development period is currently estimated as continuing through June 2020 and, as such, the $15.0 million upfront payment is being recognized ratably over this period. During the years ended December 31, 2018, 2017 and 2016, the Company recorded licensing revenue of approximately $2.0 million, $1.8 million and $6.8 million, respectively, under this agreement. Included in licensing revenue for the year ended December 31, 2018 is $0.4 million related to the accelerated recognition, as a result of the Sumitomo Amendment, of the remaining portion of deferred revenue associated with the $1.0 million upfront payment

3. Significant Agreements – (continued)

that the Company received under the Original Sumitomo Agreement in connection with Sumitomo Dainippon's exercise of the Country Option with respect to Korea.

The Company recognizes milestone payments when the associated milestones are achieved. As of December 31, 2018 and 2017, the Company had recorded deferred revenues of $2.4 million and $4.5 million, respectively, under this agreement.

4. Cash, Cash Equivalents and Investments

The following table summarizes the Company's cash, cash equivalents and investments as of December 31, 2018 and December 31, 2017:

	As of December 31, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
		(in thousands)		
Cash and cash equivalents:				
Cash and money market funds	$ 43,248	$ —	$ —	$ 43,248
Investment debt securities:				
Commercial paper	34,353	—	(26)	34,327
Corporate debt securities	349,854	27	(704)	349,177
U.S. government and agency securities	9,410	5	(7)	9,408
Total investments	393,617	32	(737)	392,912
Total cash, cash equivalents and investments	$436,865	$ 32	$(737)	$436,160

	As of December 31, 2017			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
		(in thousands)		
Cash and cash equivalents:				
Cash and money market funds	$ 70,013	$ —	$ —	$ 70,013
Investment debt securities:				
Commercial paper	2,986	—	(3)	2,983
Corporate debt securities	333,958	—	(752)	333,206
U.S. government and agency securities	8,743	—	(28)	8,715
Total investments	345,687	—	(783)	344,904
Total cash, cash equivalents and investments	$415,700	$ —	$(783)	$414,917

As of December 31, 2018, the Company held a total of twenty-four positions that were in a continuous unrealized loss position for twelve months or longer. The Company has determined that the unrealized losses are deemed to be temporary impairments as of December 31, 2018. The Company believes that the unrealized losses generally are caused by increases in the risk premiums required by market participants rather than an adverse change in cash flows or a fundamental weakness in the credit quality of the issuer or underlying assets. Because the Company has the ability and intent to hold these investments until a recovery of fair value, which may be maturity, it does not consider the investments to be other-than-temporarily impaired at December 31, 2018.

4. Cash, Cash Equivalents and Investments – (continued)

The fair value for the Company's available-for-sale investment debt securities that have been in an unrealized loss position for less than twelve months or twelve months or longer is as follows:

	As of December 31, 2018					
	Less than 12 months		12 months or longer		Total	
			(in thousands)			
	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses
Commercial paper	$ 34,327	$ (26)	$ —	$ —	$ 34,327	$ (26)
Corporate debt securities	260,547	(443)	56,626	(261)	317,173	(704)
U.S. government and agency securities	—	—	1,991	(7)	1,991	(7)
Total	$294,874	$(469)	$58,617	$(268)	$353,491	$(737)

	As of December 31, 2017					
	Less than 12 months		12 months or longer		Total	
			(in thousands)			
	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses
Commercial paper	$ 2,983	$ (3)	$ —	$ —	$ 2,983	$ (3)
Corporate debt securities	272,453	(506)	60,753	(246)	333,206	(752)
U.S. government and agency securities	6,723	(25)	1,992	(3)	8,715	(28)
Total	$282,159	$(534)	$62,745	$(249)	$344,904	$(783)

5. Fixed Assets, Net

Fixed assets are stated at cost and depreciated or amortized using the straight-line method based on useful lives as follows:

	Useful lives (Years)	December 31,	
		2018	2017
		(in thousands)	
Office equipment and software	3	$ 3,986	$ 5,048
Leasehold improvements	Over life of lease	14,464	14,665
Furniture and fixtures	7	3,907	5,257
Subtotal		22,357	24,970
Less: accumulated depreciation		(11,946)	(8,786)
Fixed assets, net		$ 10,411	$16,184

Depreciation expense for the years ended December 31, 2018, 2017 and 2016 was approximately $4.6 million, $4.6 million and $3.8 million, respectively.

6. Inventory

Inventories are stated at the lower of cost or market. Inventories consisted of the following:

	December 31,	
	2018	2017
	(in thousands)	
Work-in-process	$7,019	$3,249
Finished goods	89	231
Inventory, net	$7,108	$3,480

7. Accounts Payable, Accrued Expenses and Other Liabilities

Accounts payable, accrued expenses and other liabilities consisted of the following:

	December 31,	
	2018	2017
	(in thousands)	
Accounts payable	$ 11,765	$ 6,965
Accrued employee compensation	20,335	27,118
Accrued contracted services	54,681	51,154
Other liabilities	18,328	9,540
Accounts payable, accrued expenses and other liabilities	$105,109	$94,777

8. Long-Term Debt

Debt, net of discounts and deferred financing costs, consisted of the following:

	December 31,	
	2018	2017
	(in thousands)	
Long-term debt	$371,250	$355,677
Less current portion	—	—
Long-term debt outstanding	$371,250	$355,677

On July 6, 2016, the Company issued and sold $460.0 million aggregate principal amount of the Convertible Notes. The Company received net proceeds from the sale of the Convertible Notes of $447.6 million, after deducting underwriting discounts and estimated offering expenses of approximately $12.4 million. The Company used approximately $38.4 million of such net proceeds to fund the cost of the Capped Call Transactions (as defined below) that were entered into in connection with the issuance of the Convertible Notes.

The Convertible Notes were issued pursuant to an indenture, as supplemented by a first supplemental indenture, each dated as of July 6, 2016 (collectively, the ‘‘Indenture’’), by and between the Company and U.S. Bank National Association, as trustee. The Convertible Notes are senior unsecured obligations of the Company, bear interest at a fixed rate of 3.25% per year (payable semi-annually on January 1 and July 1 of each year, beginning on January 1, 2017) and will mature on July 1, 2023, unless earlier repurchased, redeemed or converted. Holders may convert their Convertible Notes at their option at any time prior to the close of business on the business day immediately preceding January 1, 2023 only under the following circumstances: (i) during any calendar quarter commencing after September 30, 2016, if the last reported sale price of the Company’s common stock for at least 20 trading days (whether or not consecutive) during the period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day; (ii) during the five business day period after any five consecutive trading day period in which the trading price (as defined in

8. Long-Term Debt – (continued)

the Indenture) per $1,000 principal amount of Convertible Notes for each trading day of such five consecutive trading day period was less than 98% of the product of the last reported sale price of the Company's common stock and the conversion rate on each such trading day; (iii) if the Company calls any or all of the Convertible Notes for redemption, at any time prior to the close of business on the scheduled trading day immediately preceding the redemption date; or (iv) upon the occurrence of specified corporate events. On or after January 1, 2023 until the close of business on the second scheduled trading day immediately preceding the maturity date, holders may convert their Convertible Notes at any time, regardless of the foregoing circumstances. Upon conversion of the Convertible Notes, the Company will pay or deliver, as the case may be, cash, shares of the Company's common stock (and cash in lieu of any fractional shares) or a combination of cash and shares of the Company's common stock, at the Company's election. The initial conversion rate of the Convertible Notes is 5.0358 shares of the Company's common stock per $1,000 principal amount of Convertible Notes, which is equivalent to an initial conversion price of approximately $198.58 per share of the Company's common stock. The conversion rate is subject to adjustment upon the occurrence of certain events but will not be adjusted for any accrued and unpaid interest. If the Company undergoes a fundamental change (as defined in the Indenture), holders may require the Company to repurchase for cash all or any portion of their Convertible Notes at a fundamental change repurchase price equal to 100% of the principal amount of the Convertible Notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date. In addition, if certain make-whole fundamental changes occur, the Company will, in certain circumstances, increase the conversion rate for any Convertible Notes converted in connection with such make-whole fundamental change. The Company may not redeem the Convertible Notes prior to July 6, 2021. The Company may redeem for cash all or part of the Convertible Notes, at its option, on or after July 6, 2021, if the last reported sale price of the Company's common stock has been at least 130% of the conversion price then in effect for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading day period (including the last trading day of such period) ending on, and including, the trading day immediately preceding the date on which the Company provides notice of redemption at a redemption price equal to 100% of the principal amount of the Convertible Notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date. The Indenture provides for customary events of default.

On June 30, 2016, in connection with the pricing of the Convertible Notes, the Company entered into privately-negotiated capped call transactions (the ''Base Capped Call Transactions'') with each of Royal Bank of Canada, UBS AG, London Branch, and Credit Suisse Capital LLC (the ''Option Counterparties''). On July 1, 2016, in connection with the underwriters' exercise of their over-allotment option in full, the Company entered into additional capped call transactions (the ''Additional Capped Call Transactions'' and, together with the Base Capped Call Transactions, the ''Capped Call Transactions'') with the Option Counterparties. The Capped Call Transactions are expected generally to reduce the potential dilution with respect to the Company's common stock and/or offset the cash payments the Company would be required to make in excess of the principal amount of converted Convertible Notes, as the case may be, upon conversion of the Convertible Notes in the event that the market price per share of the Company's common stock, as measured under the terms of the Capped Call Transactions, is greater than the strike price of the Capped Call Transactions, which initially corresponds to the conversion price of the Convertible Notes and is subject to anti-dilution adjustments substantially similar to those applicable to the conversion rate of the Convertible Notes. The cap price of the Capped Call Transactions is initially $262.2725 per share, and is subject to certain adjustments under the terms of the Capped Call Transactions. If, however, the market price per share of the Company's common stock, as measured under the terms of the Capped Call Transactions, exceeds the cap price of the Capped Call Transactions, there would nevertheless be dilution and/or there would not be an offset of such potential cash payments, in each case, upon conversion of the Convertible Notes to the extent that such market price exceeds the cap price of the Capped Call Transactions.

8. Long-Term Debt – (continued)

In accordance with ASC Subtopic 470-20, the Company used an effective interest rate of 8.4% to determine the liability component of the Convertible Notes. This resulted in the recognition of $334.4 million as the liability component of the Convertible Notes and the recognition of the residual $113.1 million as the debt discount with a corresponding increase to additional paid-in capital for the equity component of the Convertible Notes.

Interest expense was $30.5 million, $29.3 million and $14.2 million for the years ended December 31, 2018, 2017 and 2016, respectively, related to the Convertible Notes. Accrued interest on the Convertible Notes was approximately $7.5 million and $14.9 million as of December 31, 2018 and 2017, respectively. The Company recorded debt issuance costs of $12.4 million, which are being amortized using the effective interest method. As of December 31, 2018 and 2017, $8.8 million and $10.3 million, respectively, of debt issuance costs are recorded on the consolidated balance sheet in Long-term debt, in accordance with ASU No. 2015-03, ''Interest — Imputation of Interest (Subtopic 835-30): Simplifying the Presentation of Debt Issuance Costs.'' As of December 31, 2018 and 2017, $460.0 million aggregate principal amount of the Convertible Notes was outstanding.

9. Product Revenue, Net

The Company recognized net sales of Ocaliva of $177.8 million, $129.2 million and $18.2 million for the years ended December 31, 2018, 2017 and 2016, respectively.

The table below summarizes consolidated product revenue, net by region:

	Years Ended December 31,		
	2018	2017	2016
		(in thousands)	
Product revenue, net:			
U.S.	$140,822	$115,807	$18,169
ex-U.S.	36,960	13,368	—
Total product revenue, net	$177,782	$129,175	$18,169

10. Fair Value Measurements

The carrying amounts of the Company's receivables and payables approximate their fair value due to their short maturities.

Accounting principles provide guidance for using fair value to measure assets and liabilities. The guidance includes a three-level hierarchy of valuation techniques used to measure fair value, defined as follows:

- Unadjusted Quoted Prices — The fair value of an asset or liability is based on unadjusted quoted prices in active markets for identical assets or liabilities (Level 1).
- Pricing Models with Significant Observable Inputs — The fair value of an asset or liability is based on information derived from either an active market quoted price, which may require further adjustment based on the attributes of the financial asset or liability being measured, or an inactive market transaction (Level 2).
- Pricing Models with Significant Unobservable Inputs — The fair value of an asset or liability is primarily based on internally derived assumptions surrounding the timing and amount of expected cash flows for the financial instrument. Therefore, these assumptions are unobservable in either an active or inactive market (Level 3).

The Company considers an active market as one in which transactions for the asset or liability occur with sufficient frequency and volume to provide pricing information on an ongoing basis. Conversely, the Company

10. Fair Value Measurements – (continued)

views an inactive market as one in which there are few transactions for the asset or liability, the prices are not current, or price quotations vary substantially either over time or among market makers. Where appropriate, non-performance risk, or that of a counterparty, is considered in determining the fair values of liabilities and assets, respectively.

The Company's cash deposits and money market funds are classified within Level 1 of the fair value hierarchy because they are valued using bank balances or quoted market prices. Investments are classified as Level 2 instruments based on market pricing and other observable inputs.

Financial assets carried at fair value are classified in the tables below in one of the three categories described above:

		Fair Value Measurements Using		
	Total	Level 1	Level 2	Level 3
		(in thousands)		
December 31, 2018				
Assets:				
Money market funds (included in cash and cash equivalents)	$ 11,647	$11,647	$ —	$ —
Available-for-sale debt securities:				
Commercial paper	34,327	—	34,327	—
Corporate debt securities	349,177	—	349,177	—
U.S. government and agency securities	9,408	—	9,408	—
Total financial assets:	$404,559	$11,647	$392,912	$ —
December 31, 2017				
Assets:				
Money market funds (included in cash and cash equivalents)	$ 13,361	$13,361	$ —	$ —
Available-for-sale debt securities:				
Commercial paper	2,983	—	2,983	—
Corporate debt securities	333,206	—	333,206	—
U.S. government and agency securities	8,715	—	8,715	—
Total financial assets:	$358,265	$13,361	$344,904	$ —

The gross realized gains and losses on sales of available-for-sale investment debt securities were immaterial for the fiscal years ended December 31, 2018, 2017, and 2016.

The estimated fair value of marketable debt securities (commercial paper, corporate debt securities and U.S. government and agency securities) as of December 31, 2018 and 2017, respectively, by contractual maturity, are as follows:

	Fair Value as of December 31,	
	2018	2017
	(in thousands)	
Due in one year or less	$319,717	$282,159
Due after one year through two years	73,195	62,745
Total investments in debt securities	$392,912	$344,904

Actual maturities may differ from contractual maturities because issuers may have the right to call or prepay obligations without call or prepayment penalties.

11. Stockholders' Equity and Preferred Stock

Common Stock

On April 9, 2018, the Company issued and sold (i) 2,695,313 shares of common stock in a registered public offering (including 351,563 shares issued and sold upon the exercise in full of the underwriters' option to purchase additional shares), at a price to the public of $64.00 per share (the ''Public Offering'') and (ii) 1,562,500 shares of common stock (the ''Private Placement Shares'') in a concurrent private placement (the ''Concurrent Private Placement'') exempt from the registration requirements of the Securities Act of 1933, as amended, at a purchase price per share equivalent to the price to the public set in the Public Offering and pursuant to a securities purchase agreement (the ''Securities Purchase Agreement'') that the Company entered into with the purchasers in the Concurrent Private Placement (the ''Private Placement Purchasers''). Pursuant to the Securities Purchase Agreement, the Company granted to the Private Placement Purchasers certain registration rights requiring the Company, upon request of the Private Placement Purchasers (and/or certain affiliate transferees thereof) on or after June 5, 2018 and subject to certain terms and conditions, to register the resale by such Private Placement Purchasers (and/or such affiliates) of the Private Placement Shares held by them. As of the date of this Annual Report on Form 10-K, no Private Placement Purchaser has exercised any such registration rights.

The net proceeds to the Company from the Public Offering and the Concurrent Private Placement were approximately $261.4 million, after deducting underwriting discounts, commissions and estimated offering expenses of approximately $11.1 million.

As of December 31, 2018 and 2017, the Company had 45,000,000 authorized shares of common stock, par value $0.001 per share.

Dividends

Subject to preferences that may be applicable to any outstanding shares of preferred stock, holders of common stock are entitled to receive ratably such dividends, if any, as may be declared from time to time by the Company's board of directors out of funds legally available for dividend payments. The Company has never declared or paid any cash dividends on its common stock, and does not anticipate paying any cash dividends on its common stock in the foreseeable future. The Company intends to retain all available funds and any future earnings to fund the development and expansion of its business. Any future determination to pay dividends will be at the discretion of the board of directors and will depend upon a number of factors, including the results of operations, financial condition, future prospects, contractual restrictions, restrictions imposed by applicable law and other factors the board of directors deems relevant.

Voting

Holders of common stock are entitled to one vote for each share held with respect to all matters submitted to a vote of the stockholders and do not have cumulative voting rights.

Preferred Stock

As of December 31, 2018 and 2017, the Company had 5,000,000 authorized shares of preferred stock, par value $0.001 per share, of which none are issued.

12. Stock Compensation

The Company's 2012 Equity Incentive Plan (''2012 Plan'') became effective upon the pricing of its initial public offering in October 2012 (the ''IPO''). At the same time, the Company's 2003 Stock Incentive Plan (''2003 Plan'') was terminated and 555,843 shares available under the 2003 Plan were added to the 2012 Plan.

The estimated fair value of the options that have been granted under the 2003 Plan and the 2012 Plan was determined utilizing the Black-Scholes option-pricing model at the date of grant. The fair value of the RSUs and RSAs that have been granted under the 2012 Plan was determined utilizing the closing price of the

12. Stock Compensation – (continued)

Company's common stock on the date of grant. There were approximately 2.2 million and 1.9 million shares available for grant remaining under the 2012 Plan at December 31, 2018 and 2017, respectively. On January 1, 2018 and 2017, the number of shares available for issuance under the 2012 Plan increased by 1,010,693 and 993,558 shares, respectively, as a result of the automatic increase provisions thereof.

Stock Options and Performance-Based Stock Options

The Company estimated the fair value of stock options granted in the periods presented using a Black-Scholes option-pricing model utilizing the following assumptions:

	Years Ended December 31,		
	2018	2017	2016
Volatility	62 – 73%	61 – 65%	60 – 66%
Expected term (in years)	6.0	6.0 – 9.9	5.1 – 10.0
Risk-free rate	1.8 – 3.0%	1.8 – 2.4%	1.1 – 2.4%
Expected dividend yield	—%	—%	—%

The stock price for options granted prior to the IPO was determined based on a valuation of the Company's common stock. For options granted after the IPO, the stock price is the closing price of the Company's common stock on the date of grant. The risk-free interest rate was based on the rate for U.S. Treasury securities at the date of grant with maturity dates approximately equal to the expected term of the award at the grant date. The expected term of options granted represents the period of time the options are expected to be outstanding and is based on the simplified method. The expected volatility was estimated based on historical volatility information of publicly-traded peer companies.

The Company's combined outstanding employee and non-employee option activity for the period from December 31, 2017 through December 31, 2018 is summarized as follows:

	Number of Options (in thousands)	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2017	1,808	$114.70	7.4	$14,648
Granted	712	$ 64.98	—	$ —
Exercised	(188)	$ 25.52	—	$ —
Cancelled/forfeited	(227)	$107.07	—	$ —
Expired	(231)	$177.76	—	$ —
Outstanding at December 31, 2018	1,874	$ 97.64	7.5	$45,381
Expected to vest	1,000	$ 83.20	8.7	$25,703
Exercisable	874	$114.17	6.2	$19,678

The aggregate intrinsic value of options is calculated as the difference between the exercise price of the underlying options and the deemed fair value of the Company's common stock for those options that had exercise prices lower than the deemed fair value of the Company's common stock. The weighted-average grant date fair value of options granted in the years ended December 31, 2018, 2017 and 2016 was $41.18, $63.65 and $64.80 per option, respectively. The aggregate intrinsic value of stock options exercised during the years ended December 31, 2018, 2017 and 2016 was $14.1 million, $9.4 million and $22.0 million, respectively. As of December 31, 2018, the total compensation cost related to non-vested option awards not yet recognized is approximately $38.4 million with a weighted average remaining vesting period of 1.20 years.

12. Stock Compensation – (continued)

The Company has in the past, and may in the future, grant performance-based stock option awards with vesting terms based on the achievement of specified goals. To the extent such awards do not contain a market condition, the Company recognizes no expense until achievement of the performance requirement is deemed probable.

In April 2014, the Company issued 57,063 performance-based options to certain employees that will vest upon the achievement of certain regulatory milestones related to OCA at future dates. In November 2014, the Company issued an additional 10,839 performance-based options that will vest upon the achievement of the same regulatory milestones. As of both December 31, 2018 and 2017, the achievement of such milestones was not deemed to be probable and no stock-based compensation expense was recognized for these performance-based options.

Restricted Stock Units and Awards & Performance-Based Restricted Stock Units and Awards

The following table summarizes the aggregate RSU, RSA, performance restricted stock unit award (“PRSU”) and performance restricted share award (“PRSA”) activity for the year ended December 31, 2018:

	Number of Awards (in thousands)	Weighted Average Grant Date Fair Value
Non-vested awards at December 31, 2017	493	$113.60
Granted	612	$ 65.28
Vested	(192)	$124.69
Forfeited	(140)	$ 91.26
Non-vested awards at December 31, 2018	773	$ 76.10

For the years ended December 31, 2018, 2017 and 2016, the weighted-average grant date fair value of RSUs, RSAs, PRSUs and PRSAs granted was $65.28, $102.35 and $117.63, respectively. The total fair value of RSUs, RSAs, PRSUs and PRSAs that vested during the years ended December 31, 2018, 2017 and 2016 was $24.0 million, $16.7 million and $12.8 million, respectively. As of December 31, 2018, there was $44.5 million of unrecognized compensation expense related to unvested RSUs, RSAs, PRSUs, and PRSAs, which is expected to be recognized over a weighted average period of 1.27 years.

During the year ended December 31, 2018, the Company granted a total of 51,200 PRSUs and 4,300 PRSAs to certain of the Company’s executive officers. The performance criterion for such PRSUs and PRSAs is based on the Total Shareholder Return (“TSR”) of the Company’s common stock relative to the TSR of the companies comprising the S&P Biotechnology Select Industry Index (the “TSR Peer Group”) over a 3-year performance period and is accounted for as a market condition under ASC 718. The TSR for the Company or a member of the TSR Peer Group is calculated by dividing (a) the difference of the ending average stock price minus the beginning average stock price by (b) the beginning average stock price. The beginning average stock price equals the average closing stock price over the one calendar month period prior to the beginning of the performance period, after adjusting for dividends, as applicable. The ending average stock price equals the average closing price over the one calendar month period ending on the last day of the performance period, after adjusting for dividends, as applicable. The Company’s relative TSR is then used to calculate the payout percentage, which may range from zero percent (0%) to one hundred and fifty percent (150%) of the target award. The Company utilized a Monte Carlo Simulation to determine the grant date fair value of such PRSUs and PRSAs. The Company recorded approximately $1.3 million of stock-based compensation related to such PRSUs and PRSAs during the year ended December 31, 2018. No PRSUs or PRSAs were granted during the year ended December 31, 2017.

The Company accounts for all forfeitures when they occur. Ultimately, the actual expense recognized over the vesting period will be for only those shares that vest and are not forfeited. The Company has in the

12. Stock Compensation – (continued)

past, and may in the future, grant performance-based awards with vesting terms based on the achievement of specified goals. To the extent such awards do not contain a market condition, the Company recognizes no expense until achievement of the performance requirement is deemed probable.

Stock-based compensation expense has been reported in the Company's statements of operations as follows:

	Years Ended December 31,		
	2018	2017	2016
		(In thousands)	
Selling, general and administrative	$38,361	$40,004	$32,073
Research and development	11,553	16,964	14,132
Total stock-based compensation	$49,914	$56,968	$46,205

13. Employee Benefit Plans

The Company maintains a defined contribution plan, which is qualified under section 401(k) of the Internal Revenue Code for U.S. employees. Employees may make contributions by withholding a percentage of their salary up to the Internal Revenue Service annual limit of $18,500 and $24,500 in 2018 for employees under 50 years old and employees 50 years old or over, respectively. The Company's matching contribution vests over four years from the start of employment. The Company made approximately $1.9 million, $2.7 million and $2.3 million in matching contributions for the years ended December 31, 2018, 2017 and 2016, respectively.

14. Income Taxes

The components of loss before income taxes for the years ended December 31, 2018, 2017 and 2016 includes the following:

	Years Ended December 31,		
	2018	2017	2016
		(in thousands)	
United States	$ (72,655)	$(102,586)	$(154,812)
Foreign	(236,587)	(257,781)	(258,018)
Total	$(309,242)	$(360,367)	$(412,830)

Income tax expense (benefit) differed from the amounts computed by applying the statutory U.S. Federal income tax rate of 21% (34% for 2017 and 2016) to loss before income taxes as a result of the following:

	Years Ended December 31,		
	2018	2017	2016
		(in thousands)	
Computed "expected" tax benefit	$(64,941)	$(122,525)	$(140,362)
State taxes, net of U.S. Federal benefit	—	—	—
U.S. Federal rate reduction	—	84,787	—
U.S. Federal valuation allowance	9,352	282	40,377
Stock-based compensation	6,423	(49,391)	5,161
Officer compensation	22	26	50
Foreign valuation allowance	44,896	52,521	57,759
Foreign tax rate differences	4,787	35,125	37,142
Other	(539)	(825)	(127)
Total	$ —	$ —	$ —

14. Income Taxes – (continued)

The tax effects of temporary differences that give rise to the deferred tax assets and liabilities at December 31, 2018 and 2017 are presented below:

	December 31,	
	2018	2017
	(in thousands)	
Deferred tax assets:		
Net operating loss and other carryforwards	$ 329,088	$ 276,481
Stock compensation	13,228	14,651
Deferred revenue	620	1,149
Accrued compensation	3,431	3,994
Accrued expense	2,340	1,139
Intellectual property	—	1,059
Interest limitation	2,913	—
Other	1,021	492
Deferred tax assets before valuation allowance	352,641	298,965
Valuation allowance	(338,852)	(282,730)
Total deferred tax assets	13,789	16,235
Deferred tax liabilities:		
Convertible Note	(13,789)	(16,235)
Total deferred tax liabilities	(13,789)	(16,235)
Net deferred tax asset (liability)	$ —	$ —

Effects of the Tax Cuts and Jobs Act

In late 2017, the United States enacted the Tax Cuts and Jobs Act of 2017 (the ''TCJA''), which significantly changed U.S. tax law by implementing a reduction in the corporate tax rate to 21%, moving from a worldwide tax system to a territorial system and imposing new or additional limitations on the deductibility of interest expense and executive compensation.

Given the significance of the legislation, the staff of the U.S. Securities and Exchange Commission (the ''SEC'') issued Staff Accounting Bulletin No. 118 (''SAB 118''), which allowed registrants to record provisional amounts during a one year ''measurement period'' similar to that used when accounting for business combinations. The Company applied the guidance in SAB 118 when accounting for the enactment-date effects of the TCJA in 2017 and throughout 2018.

For the year ended December 31, 2017, amounts recorded principally related to the reduction in the U.S. corporate income tax rate to 21%, which resulted in the Company reducing its net deferred tax asset and associated valuation allowance by $82.8 million. Additionally, the new law included a one-time mandatory repatriation transition tax on the net accumulated earnings and profits of a U.S. taxpayer's foreign subsidiaries. As a result of accumulated losses since inception, there was no income tax effect.

At December 31, 2018, the Company completed its accounting of SAB 118 for all of the enactment-date income tax effects of the TCJA. The Company has not made any measurement-period adjustments and there were no additional material adjustments related to the TCJA.

Net Operating Losses

As of December 31, 2018 and 2017, the Company had net operating loss carryforwards (''NOLs'') for U.S. Federal income tax purposes of $658.4 million and $628.0 million, respectively. The enactment of the TCJA in late 2017 modified the ability of companies to utilize NOLs arising in tax years beginning on or after

14. Income Taxes – (continued)

January 1, 2018 by providing that such NOLs may be carried-forward indefinitely and used to offset up to 80 percent of taxable income in any given future year. Existing NOLs that arose in tax years beginning prior to January 1, 2018 were not affected by the TCJA and are generally eligible to be carried-forward for up to 20 years and used to fully offset taxable income in future years. The Company's pre-2018 NOLs will expire for U.S. Federal income tax purposes between 2024 and 2037. The Company also has certain state and foreign NOLs in varying amounts depending on the different state and foreign tax laws.

In addition, the Company's ability to utilize its NOLs may be limited under Section 382 of the Internal Revenue Code or similar rules. The Section 382 limitations apply if an ''ownership change'' occurs. Generally, an ownership change occurs when certain shareholders increase their aggregate ownership by more than 50 percentage points over their lowest ownership percentage in a testing period (typically three years). The Company has evaluated whether one or more ownership changes under Section 382 have occurred since its inception and has determined that there have been at least two such changes. Although the Company believes that these ownership changes have not resulted in material limitations on its ability to use these NOLs, its ability to utilize these NOLs may be limited due to future ownership changes or for other reasons. As a result, the Company may not be able to take full advantage of its carryforwards for U.S. Federal, state, and foreign tax purposes.

Valuation Allowance

At December 31, 2018 and 2017, the Company maintained a full valuation allowance on its deferred tax assets since it has not yet achieved sustained profitable operations. As a result, the Company has not recorded any income tax benefit since its inception. In 2018, the valuation allowance for deferred tax assets increased by approximately $56.1 million. This includes an increase of $9.4 million, $1.9 million and $44.9 million for U.S. Federal, state and foreign tax, respectively, partially offset by a decrease of $0.1 million to equity. In 2017, the valuation allowance for deferred tax assets increased by approximately $59.3 million. This includes an increase of $0.3 million, $6.8 million and $52.5 million for U.S. Federal, state and foreign tax, respectively, partially offset by a decrease of $0.3 million to equity.

Unrecognized Tax Benefits

At December 31, 2018 and 2017, the Company had no reserves for unrecognized tax benefits.

The Company and its subsidiaries are subject to taxation in the United States and various foreign jurisdictions. Of the major jurisdictions, the Company is subject to examination in: the United States for U.S. Federal purposes for 2015 and forward and generally for state purposes for 2014 and forward; and the United Kingdom for 2016 and forward. However, NOLs are subject to audit in any tax year in which those losses are utilized, notwithstanding the year of origin.

15. Commitments and Contingencies

Facility Leases

In May 2014, the Company entered into a lease agreement with respect to office space in San Diego, California. The Company leases approximately 47,000 square feet of space at this property. The lease covering this property is scheduled to expire in July 2020.

In January 2016, Intercept Pharma Europe Ltd. (''IPEL''), a wholly owned subsidiary of the Company, entered into an underlease with respect to office space in London, United Kingdom. The Company is the guarantor to the underlease. IPEL leases approximately 8,500 square feet of space at this property. The lease covering this property is scheduled to expire in May 2024.

In December 2016, the Company entered into a lease agreement with respect to office space at 10 Hudson Yards in New York, New York, where the Company's corporate headquarters are located. The Company leases an aggregate of approximately 41,100 square feet of office space at this property. The lease covering this property is scheduled to expire at varying times through June 2021.

15. Commitments and Contingencies – (continued)

The Company also leases office space in several other locations.

Rent expense under operating leases for facilities for the years ended December 31, 2018, 2017 and 2016 was approximately $6.3 million, $8.9 million and $5.5 million, respectively. As of December 31, 2018, minimum contractually-obligated operating lease cash payments under non-cancelable leases, as amended, are as follows:

Year Ending December 31,	Amount
	(in thousands)
2019	$ 9,506
2020	8,126
2021	4,841
2022	2,945
2023	2,982
Thereafter	1,531
Total future minimum operating lease payments	$29,931

Purchase Commitments

The Company enters into contracts in the normal course of business with contract research organizations for its clinical trials, contract manufacturing organizations for the manufacture and supply of its clinical and commercial product needs and other vendors for other research and development and commercial activities, as well as services and products for operating purposes. The Company's agreements generally provide for termination with notice. Such agreements are cancelable contracts are not included as purchase commitments. The Company has included as purchase obligations its commitments under agreements to the extent they are quantifiable and are not cancelable. The Company had purchase obligations of approximately $29.8 million as of December 31, 2018.

Legal Proceedings

The Company is involved in various disputes, governmental inquiries and investigations, legal proceedings and litigation in the course of its business, including the matters described below and, from time to time, intellectual property, employment and other litigation. These matters, which could result in damages, fines or other administrative, civil or criminal remedies, liabilities or penalties, are often complex and the outcome of such matters is often uncertain. The Company may from time to time enter into settlements to resolve such matters.

On September 27, 2017, a purported shareholder class action, initially styled DeSmet v. Intercept Pharmaceuticals, Inc., et al, was filed in the United States District Court for the Southern District of New York, naming the Company and certain of its officers as defendants. The Court appointed lead plaintiffs in the lawsuit on June 1, 2018, and the lead plaintiffs filed an amended complaint on July 31, 2018, captioned Hou Liu and Amy Fu v. Intercept Pharmaceuticals, Inc., et al., naming the Company and certain of its current and former officers as defendants. The lead plaintiffs claim to be suing on behalf of anyone who purchased or otherwise acquired the Company's common stock between June 9, 2016 and September 20, 2017. This lawsuit alleges that material misrepresentations and/or omissions of material fact were made in the Company's public disclosures during the period from June 9, 2016 to September 20, 2017, in violation of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended (the ''Exchange Act''), and Rule 10b-5 promulgated thereunder. The alleged improper disclosures relate to statements regarding Ocaliva dosing, use and pharmacovigilance-related matters, as well as the Company's operations, financial performance and prospects. The plaintiffs seek unspecified monetary damages on behalf of the putative class, an award of costs and expenses, including attorney's fees, and rescissory damages. On September 14, 2018, the Company filed a motion to dismiss the amended complaint. Separately, on January 5, 2018, a follow-on derivative suit, styled

15. Commitments and Contingencies – (continued)

Davis v. Pruzanski et al., was filed in New York state court by shareholder Gregg Davis based on substantially the same allegations as those set forth in the securities case. On December 1, 2017, a purported shareholder demand was made on the Company based on substantially the same allegations as those set forth in the securities case.

While the Company believes that it has a number of valid defenses to the claims described above and intends to vigorously defend itself, the matters are in the early stages of litigation and no assessment can be made as to the likely outcome of the matters or whether they will be material to the Company. Accordingly, an estimate of the potential loss, or range of loss, if any, to the Company relating to the matters is not possible at this time.

In May 2018, the Company received a subpoena from the SEC requesting information in connection with the Company's patient assistance program and certain of the Company's commercial activities. The SEC's letter enclosing the subpoena states that the investigation and the subpoena do not mean that the Company or anyone else has broken the law, or that the SEC has a negative opinion of any person, entity or security. The Company is cooperating fully with the SEC in this matter. At this time, the Company is unable to predict whether any proceeding may be instituted in connection with the subpoena, or the outcome of any such proceeding, if instituted.

In August 2018, the Company received an inquiry from the U.S. Department of Justice acting through the U.S. Attorney's office for the District of Massachusetts (the ''DOJ'') requesting the voluntary production of certain information regarding the Company's activities and public statements concerning Ocaliva's dosing, use, adverse events, marketing and reimbursement. The Company cooperated fully with the DOJ in connection with this inquiry and in early 2019 the DOJ informed the Company that it had reviewed the information produced by the Company and did not plan to request further information in connection therewith. Subsequently, a qui tam complaint alleging that the Company violated federal and state false claims acts was unsealed in January 2019. The qui tam complaint was voluntarily dismissed without prejudice by the relator with the consent of the United States of America and various named state government plaintiffs.

16. Net Loss Per Share

Basic loss per share is computed by dividing net loss attributable to common stockholders (numerator) by the weighted average number of common shares outstanding (denominator) during the period. For the years ended December 31, 2018, 2017 and 2016, as the Company was in a net loss position, the diluted loss per share computations for such periods did not assume the conversion of the Convertible Notes, exercise of stock options or vesting of RSUs as they would have had an anti-dilutive effect on loss per share.

The following potentially dilutive securities have been excluded from the computations of diluted weighted average shares outstanding as of December 31, 2018, 2017 and 2016, as the inclusion thereof would have been anti-dilutive:

	December 31,		
	2018	2017	2016
		(in thousands)	
Convertible Notes	2,316		
Options	1,874	1,808	1,553
Restricted stock units	441	493	382
Total	4,631	2,301	1,935

17. Quarterly Financial Data (unaudited)

The following table summarizes the unaudited quarterly financial data for the years ended December 31, 2018 and 2017:

	Quarters Ended				
	March 31,	June 30,	September 30,	December 31,	Total
	(in thousands, except for per share amounts)				
2018					
Revenues	$ 35,963	$ 43,575	$ 46,986	$ 53,280	$ 179,804
Operating loss	(75,456)	(69,777)	(58,286)	(81,971)	(285,490)
Net loss	(81,590)	(75,193)	(64,454)	(88,005)	(309,242)
Net loss per common share – basic and diluted	$ (3.22)	$ (2.58)	$ (2.18)	$ (2.97)	
2017					
Revenues	$ 21,048	$ 30,887	$ 41,334	$ 37,687	$ 130,956
Operating loss	(83,963)	(80,509)	(66,171)	(104,969)	(335,612)
Net loss	(89,930)	(86,564)	(72,601)	(111,272)	(360,367)
Net loss per common share – basic and diluted	$ (3.61)	$ (3.46)	$ (2.89)	$ (4.43)	

18. Prior Settlement

In February 2014, two purported shareholder class actions, styled *Scot H. Atwood v. Intercept Pharmaceuticals, Inc. et al.* and *George Burton v. Intercept Pharmaceuticals, Inc. et al.*, were filed in the United States District Court for the Southern District of New York, naming the Company and certain of its officers as defendants. These lawsuits were filed by stockholders who claimed to be suing on behalf of anyone who purchased or otherwise acquired the Company's securities between January 9, 2014 and January 10, 2014.

The lawsuits alleged that the Company made material misrepresentations and/or omissions of material fact in its public disclosures during the period from January 9, 2014 to January 10, 2014, in violation of Sections 10(b) and 20(a) of the Exchange Act and Rule 10b-5 promulgated thereunder. The alleged improper disclosures related to the Company's January 9, 2014 announcement that the FLINT trial had been stopped early based on a pre-defined interim efficacy analysis. Specifically, the lawsuits claimed that the January 9, 2014 announcement was misleading because it did not contain information regarding certain lipid abnormalities seen in the FLINT trial in OCA-treated patients compared to placebo.

A lead plaintiff was subsequently appointed by the Court and in June 2014, the lead plaintiff filed an amended complaint on behalf of the putative class seeking unspecified monetary damages on behalf of the putative class and an award of costs and expenses, including attorneys' fees. In August 2014, the defendants filed a motion to dismiss the complaint. In March 2015, the defendants' motion to dismiss was denied by the Court. The defendants answered the amended complaint in April 2015. In July 2015, the plaintiff moved for class certification and appointment of class representatives and class counsel. In September 2015, the defendants opposed the plaintiff's class certification motion. The plaintiff filed its reply to the defendants' opposition in October 2015, to which the defendants filed a sur-reply in November 2015. Oral arguments on the class certification motion were held in January 2016.

In May 2016, the defendants reached an agreement with the lead plaintiff to seek Court approval of a proposed resolution, the plaintiffs moved for preliminary approval of the proposed settlement and the Court entered an order preliminarily approving the settlement. The Court ordered that notice be provided to the class and preliminarily approved the proposed settlement, including the payment of $55.0 million, of which $10.0 million was agreed to be funded by the Company's insurers. The one-time net expense of $45.0 million

18. Prior Settlement – (continued)

was recorded to selling, general, and administrative expenses in the statement of operations for the year ended December 31, 2016. The settlement was paid into escrow in June 2016, with distribution to the class to occur after the Court had finally approved the settlement and the plan of allocation of those proceeds. In September 2016, the Court granted final approval of the settlement. The final judgment and order of the Court included a dismissal of the action with prejudice against all defendants. The defendants did not admit any liability as part of the settlement.

19. Restructuring Charges

In December 2017, the Company initiated a 15% reduction in the workforce and concurrently notified the affected employees. The reduction in force supports the Company's strategy to fund its development organization with strategic collaborations and to focus the Company's resources to progress its development and commercialization initiatives. The actions associated with the reductions were substantially completed during the fourth quarter of 2017 and, as a result of the reductions, the Company recorded a one-time restructuring charge of $5.2 million for termination benefits in the same period. Of this charge, $3.9 million was recorded in selling, general and administrative expense and $1.3 million was recorded in research and development expense. The restructuring charge associated with cash payments of $5.2 million were paid out in the first quarter of 2018.

No restructuring charges were incurred for the year ended December 31, 2018.

Exhibit 21.1

SUBSIDIARIES OF THE REGISTRANT

Name	Jurisdiction of Incorporation or Organization
Intercept Pharma International Limited	Republic of Ireland
Intercept Pharmaceuticals, LLC	Delaware
Intercept Italia S.r.l.	Italy
Intercept Pharma Europe Ltd.	England and Wales
Intercept Pharma UK & Ireland Ltd	England and Wales
Intercept Pharma Ltd	England and Wales
Intercept Pharma Canada Inc.	British Columbia
Intercept Pharma Switzerland GmbH	Switzerland
Intercept Pharma Deutschland GmbH	Germany
Intercept Pharma France SAS	France
Intercept Pharma Austria GmbH	Austria
Intercept Pharma Spain, S.L.U.	Spain
Intercept Pharma Portugal Unipessoal Lda	Portugal
Intercept Pharma Danmark ApS	Denmark
Intercept Pharma Nederland B.V.	The Netherlands

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

The Board of Directors
Intercept Pharmaceuticals, Inc.:

We consent to the incorporation by reference in the registration statements (No. 333-184810, No. 333-188064, No. 333-206247, No. 333-217863, and No. 333-226405) on Form S-8 and (No. 333-194974 and No. 333-217861) on Form S-3 of Intercept Pharmaceuticals, Inc. of our reports dated March 1, 2019, with respect to the consolidated balance sheets of Intercept Pharmaceuticals, Inc. as of December 31, 2018 and 2017, the related consolidated statements of operations, comprehensive loss, changes in stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2018, and the related notes (collectively, the ''consolidated financial statements''), and the effectiveness of internal control over financial reporting as of December 31, 2018, which reports appear in the December 31, 2018 annual report on Form 10-K of Intercept Pharmaceuticals, Inc.

/s/ KPMG LLP

New York, New York
March 1, 2019

Exhibit 31.1

CERTIFICATION

I, Mark Pruzanski, M.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of Intercept 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 1, 2019

/s/ Mark Pruzanski, M.D.

Mark Pruzanski, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

I, Sandip Kapadia, certify that:

1. I have reviewed this Annual Report on Form 10-K of Intercept 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 1, 2019

/s/ Sandip Kapadia

Sandip Kapadia
Chief Financial Officer and Treasurer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the ''Exchange Act''), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Mark Pruzanski, M.D., President and Chief Executive Officer of Intercept Pharmaceuticals, Inc. (the ''Company''), and Sandip Kapadia, Chief Financial Officer and Treasurer of the Company, each hereby certifies that, to the best of his knowledge:

(1) The Company's Annual Report on Form 10-K for the year ended December 31, 2018, to which this Certification is attached as Exhibit 32.1 (the ''Periodic Report''), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

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

Dated: March 1, 2019

/s/ Mark Pruzanski, M.D.
Mark Pruzanski, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Dated: March 1, 2019

/s/ Sandip Kapadia
Sandip Kapadia
Chief Financial Officer and Treasurer
(Principal Financial Officer)

A signed original of this written statement required by Rule 13a-14(b) of the Exchange Act and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350) has been provided to Intercept Pharmaceuticals, Inc. and will be retained by Intercept Pharmaceuticals, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.

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

Executive Officers

Mark Pruzanski, M.D.
President and
Chief Executive Officer

Jerome Durso
Chief Operating Officer

Lisa Bright
President, International

Gail Cawkwell, M.D., Ph.D.
SVP, Medical Affairs, Safety
& Pharmacovigilance

David Ford
Chief Human Resources Officer

Sandip Kapadia
Chief Financial Officer
and Treasurer

Richard Kim
President, U.S. Commercial
& Strategic Marketing

David Shapiro, M.D.
Chief Medical Officer

Ryan Sullivan
General Counsel and Secretary

Christian Weyer, M.D., M.A.S.
EVP, Research & Development

Board of Directors

Paolo Fundarò
Chief Financial Officer
Genextra S.p.A.

Mark Pruzanski, M.D.
President and
Chief Executive Officer

Srinivas Akkaraju, M.D., Ph.D.
Managing General Partner
Samsara BioCapital

Luca Benatti, Ph.D.
Chief Executive Officer
and Director
EryDel S.p.A.

Daniel Bradbury
Chairman and
Chief Executive Officer
Equillium, Inc.

Keith Gottesdiener, M.D.
Chief Executive Officer
and Director
Rhythm Pharmaceuticals, Inc.

Nancy Miller-Rich
Former SVP, Global Human Health
Business Development &
Licensing, Strategy and
Commercial Support
Merck & Co., Inc.

Gino Santini
Former SVP, Corporate Strategy
and Business Development
Eli Lilly and Company

Glenn Sblendorio
President, Chief Executive Officer
and Director
IVERIC bio, Inc.

Daniel Welch
Former Executive Partner
Sofinnova Ventures

Company Headquarters

10 Hudson Yards, 37th Floor
New York, NY 10001
(646) 747-1000
www.interceptpharma.com

Transfer Agent

VStock Transfer, LLC
18 Lafayette Place
Woodmere, NY 11598
(855) 987-8625 (Toll Free)
(212) 828-8436
www.vstocktransfer.com

Independent Registered Public Accounting Firm

KPMG LLP
New York, NY

Annual Meeting

The 2019 Annual Meeting of
Stockholders will be held on
Thursday, June 20, 2019 at the
offices of Skadden, Arps, Slate,
Meagher & Flom LLP, located at:
Four Times Square
New York, NY 10036

Intercept's common stock trades on the Nasdaq Global Select Market under the symbol "ICPT"