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

FORM 10-K

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

For the fiscal year ended December 31, 2017

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 FL New York, NY	**10001**
(Address of Principal Executive Offices)	(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, $0.001 par value	**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 Exchange 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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files).Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K 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, 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	☐ (Do not check if a smaller reporting company)	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 Exchange Act).Yes ☐ No ☒

The aggregate market value of the registrant's voting and non-voting common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) computed by reference to the price at which the common stock was last sold on June 30, 2017 was approximately $998,888,156. As of December 31, 2017, there were 25,172,678 shares of common stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A in connection with its 2018 Annual Meeting of Stockholders. Portions of such proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K.

TABLE OF CONTENTS

Forward-Looking Statements

This Annual Report on Form 10-K, or Annual Report, contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among other things, statements about:

- our ability to successfully commercialize Ocaliva (obeticholic acid, or OCA) in primary biliary cholangitis, or PBC;
- our ability to maintain our regulatory approval of Ocaliva in PBC in the United States, Europe, Canada and other jurisdictions in which we have or may receive marketing authorization;
- the initiation, cost, timing, progress and results of our development activities, preclinical studies and clinical trials;
- the timing of and our ability to obtain regulatory approval of OCA in indications other than PBC and regulatory approval of any other product candidates we may develop;
- 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 in the label of any products or product candidates;
- our plans to research, develop and commercialize our products and product candidates;
- our ability to obtain and maintain intellectual property protection for our products and product candidates;
- our ability to successfully commercialize our products and product candidates;
- the size and growth of the markets for our products and product candidates and our ability to serve those markets;
- the rate and degree of market acceptance of any of our products, which may be affected by the reimbursement received from payors;
- the success of competing drugs that are or become available;
- regulatory developments in the United States and other countries;
- the performance of our third-party suppliers and manufacturers;
- our collaborators' election to pursue research, development and commercialization activities;
- our ability to attract collaborators with development, regulatory and commercialization expertise;
- our need for and ability to obtain additional financing;
- our estimates regarding expenses, revenues and capital requirements and the accuracy thereof;
- our use of cash and short term investments; and
- our ability to attract and retain key scientific or management personnel.

These forward-looking statements are only predictions and we may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, so you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our business, financial condition and operating results. We have included important factors in the cautionary statements included in this Annual Report, particularly in Item 1.A. "Risk Factors," that could cause actual future results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report and the documents that we have filed as exhibits to this Annual Report with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements whether as a result of new information, future events or otherwise, except as required by applicable law.

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 Intercept Pharmaceuticals, Inc. in the United States and/or other countries. All other trademarks, service marks or other tradenames appearing in this Annual Report are the property of their respective owners.

Part I

All brand names or trademarks appearing in this Annual Report are the property of their respective holders. Unless the context requires otherwise, references in this Annual Report to "Intercept," the "Company," "we," "us," and "our" refer to Intercept Pharmaceuticals, Inc. and its consolidated subsidiaries.

Item 1. Business

Overview

We are a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat non-viral, progressive liver diseases with high unmet medical need utilizing our proprietary bile acid chemistry. Our one marketed product, OCA, and portfolio of clinical product candidates have the potential to treat orphan and more prevalent liver diseases for which, currently, there are limited therapeutic solutions.

OCA was approved in the United States in May 2016 for use in patients with PBC, under the brand name Ocaliva® (obeticholic acid). 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 the farnesoid X receptor, or FXR. We believe OCA has broad liver-protective properties and may effectively counter a variety of chronic insults to the liver that cause fibrosis, or scarring, which can eventually lead to cirrhosis, liver transplant and death. We commenced sales and marketing of Ocaliva in the United States shortly after receiving such marketing approval, and Ocaliva is now available to patients primarily through a network of specialty pharmacy distributors. 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. We have submitted or are in the process of submitting dossiers to a number of reimbursement authorities in the European Union. In May 2017, Health Canada granted a conditional approval for Ocaliva in PBC and we commenced our commercial launch in July 2017. We also plan to file for marketing authorization for OCA in PBC in other target markets.

We are currently evaluating our future development strategy for OCA in other indications, including a variety of other non-viral progressive liver diseases such as nonalcoholic steatohepatitis, or NASH, primary sclerosing cholangitis, or PSC, and biliary atresia.

OCA achieved the primary endpoint in a Phase 2b clinical trial for the treatment of NASH, known as the FLINT trial, which was sponsored by the U.S. National Institute of Diabetes and Digestive and Kidney Diseases, or NIDDK, a part of the National Institutes of Health. The FLINT trial was completed in late July 2014. We have an ongoing Phase 3 clinical trial in non-cirrhotic NASH patients with liver fibrosis, known as the REGENERATE trial. REGENERATE includes a pre-planned histology-based interim analysis after 72 weeks of treatment. In May 2017, we completed enrollment of the interim analysis cohort for the REGENERATE trial. We anticipate top-line results from the interim analysis in the first half of 2019. We have also completed a Phase 2 clinical trial, known as the 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. We announced that this trial met its primary endpoint in July 2017. We 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, which we announced in February 2018.

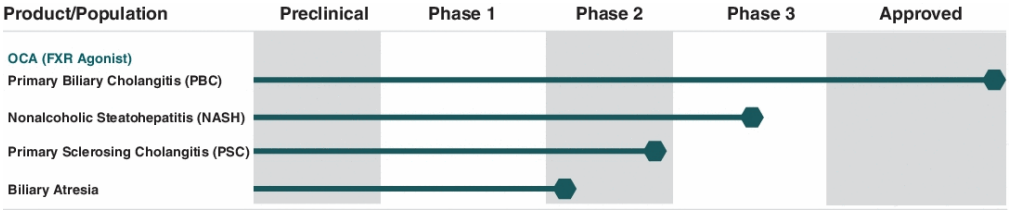
In addition to PBC and NASH, we continue to invest in research of OCA for additional patient populations with other liver diseases. For example, in July 2017, we announced top-line results of our Phase 2 AESOP trial in PSC which evaluated the effects of 24 weeks of treatment with varying doses of OCA compared to placebo. This trial achieved its primary endpoint, which we believe establishes a proof-of-concept of OCA in a second cholestatic liver disease. We plan to discuss these results with regulatory authorities to formulate our future development plans for OCA in PSC.OCA has received orphan drug designation in the United States and the European Union for the treatment of PBC and PSC and breakthrough therapy designation from the U.S. Food and Drug Administration, or FDA, for the treatment of NASH patients with liver fibrosis.

For information regarding our financial performance, including net product sales for Ocaliva in PBC and expenditures on research, development and clinical trials, refer to Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations." Financial information related to our significant customers is set forth in Note 3, "Concentration of Credit Risk" and "Accounts Receivable" to our consolidated financial statements included in this Annual Report. Other financial information such as our total assets, net loss and operating expenses can be found in our consolidated financial statements included elsewhere in this Annual Report.

The development and commercialization of pharmaceutical drugs involves a high degree of risk and investment, and the status, timing and scope of our development programs are subject to change. Important factors that could adversely affect our business are discussed in the "Risk Factors" section of this Annual Report.

OCA Development on Liver Diseases with Limited/No Approved Therapies

The following chart shows the current stage of development of OCA in different patient populations:



Our current patents for OCA are scheduled to expire at various times through 2033. We own or have rights to various trademarks, copyrights and trade names used in our business, including rights to OCA worldwide except for China, where we have exclusively licensed OCA to Sumitomo Dainippon Pharma Co. Ltd., or Sumitomo Dainippon.

By virtue of our patent portfolio and the proprietary know-how of our employees and our collaborators at the University of Perugia, we believe that we hold a leading position in the fields of bile acid chemistry and therapeutics. Starting with OCA and its underlying patents, which were assigned to us under our agreements with Professor Roberto Pellicciari, Ph.D., one of our co-founders, other researchers and the University of Perugia, our collaboration has resulted in a pipeline of bile acid analogs in addition to OCA. Through our collaboration with Professor Pellicciari and TES Pharma Srl, we are continuing our research to rationally design compounds that bind selectively and potently to FXR and other bile acid receptors.

Ocaliva Label Update

In the course of our post-marketing pharmacovigilance activities, deaths have been reported in PBC patients prescribed OCA with moderate or severe hepatic impairment. In an analysis performed by us and in consultation with the FDA, we concluded that 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 healthcare provider letter and the FDA also subsequently issued its own safety communication to reinforce recommended dosing in accordance with the Ocaliva label. Both communications reminded 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 reinforce the 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 are working with relevant regulatory authorities, including the European Medicines Agency, or EMA, to ensure that the Ocaliva label in such jurisdictions sufficiently reinforces the importance of appropriate dosing in patients with advanced cirrhosis.

Our Strategy

Our strategy is to develop and commercialize novel therapeutics for patients with progressive non-viral liver diseases, beginning with OCA for the treatment of PBC, NASH and other follow-on indications that we believe are underserved by existing marketed therapies. The key elements of our strategy are to:

- commercialize OCA in the United States, Europe, Canada and other countries, initially for the treatment of PBC;
- continue to develop OCA for the treatment of NASH and seek regulatory approval of OCA in this indication;
- continue to develop OCA in other orphan and more prevalent liver diseases; and
- maintain infrastructure and personnel in the United States and internationally to support our product development and commercialization efforts, as well as our operations as a public company.

In order to achieve our strategic objectives, we have, and will remain, focused on hiring and retaining a highly skilled management team and employee base with extensive experience and specific skill sets relating to the selection, development and commercialization of therapies for liver diseases with high unmet medical need.

Overview of Liver Function, Bile Acids and Chronic 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, or 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 and PSC 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.

Ocaliva

Overview

OCA was approved in the United States in May 2016 under the accelerated approval pathway for use in patients with PBC under the brand name Ocaliva. We commenced sales and marketing of Ocaliva in the United States shortly after receiving such marketing approval, and Ocaliva is now available to patients primarily through a network of specialty pharmacy distributors. In December 2016, the European Commission granted conditional approval for Ocaliva for the treatment of PBC and we commenced our European commercial launch in certain markets in January 2017. We have submitted or are in the process of submitting

dossiers to a number of reimbursement authorities in the European Union. In May 2017, Health Canada granted a conditional approval for Ocaliva in PBC and we commenced our commercial launch in Canada in July 2017.

Primary Biliary Cholangitis (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 damage liver cells. These damaged liver cells, in turn, release abnormal amounts of serum alkaline phosphatase, or ALP, a liver enzyme that is a key biomarker of the disease pathology. As shown in numerous clinical trials of treatment with ursodeoxycholic acid, 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.

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, or itching, 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 anti-mitochondrial antibody, or 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.

Ocaliva Phase 3 Clinical Trial in PBC

The approval of Ocaliva in the United States, Europe and Canada was supported by the results of the pivotal Phase 3 POISE trial, which was completed in March 2014. The POISE data 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, or 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 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 significant 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.

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, to support post-marketing regulatory requirements. The goal of the 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 ursodiol or who are unable to tolerate ursodiol. In this trial, eligible patients with PBC continue their ursodiol treatment, except for those patients unable to tolerate ursodiol, and are being randomized into one of two treatment arms of approximately 215 patients each. Patients are randomized to receive either placebo or 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, or 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.

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. Finally, we have also agreed to develop and characterize a lower dose formulation of Ocaliva to allow for once daily dosing in patients with moderate or severe hepatic impairment. Full approval for Ocaliva in PBC may be contingent upon the verification and description of clinical benefit in confirmatory trials.

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 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 healthcare provider letter, or 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 have taken actions to enhance education about appropriate use of Ocaliva. These initiatives include: 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 completing adjudication of all 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 reinforce the 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 are working with relevant regulatory authorities, including the European Medicines Agency, or EMA, to ensure that the Ocaliva label in such jurisdictions sufficiently reinforces the importance of appropriate dosing in patients with advanced cirrhosis.

PBC Market Opportunity

Prior to Ocaliva, the only approved drug for the treatment of PBC was ursodeoxycholic acid, available generically as ursodiol, which is widely considered the standard first line therapy for PBC patients. In patients for whom ursodiol is effective, the treatment slows the progression of PBC, reducing the likelihood of liver failure and the need for transplant.

According to our analysis of 2016 industry data, there are approximately 290,000 people with PBC in our target markets, consisting of the United States, certain European countries, Canada, Australia and New Zealand. Based on our analysis of this 2016 data, we believe approximately 119,000 patients in our target markets have been diagnosed and are under the care of a physician for PBC. We are focusing our commercial efforts on the estimated 37,000 diagnosed PBC patients who have elevated ALP levels of at least 1.67 times ULN, despite receiving treatment with ursodiol. Of those PBC patients, approximately 15,000 are estimated to be in the United States and 22,000 in our target countries outside of the United States. In addition, we believe another 8,000 patients in our target countries, including approximately 4,000 patients in the United States, are intolerant to ursodiol or have discontinued ursodiol treatment due to lack of efficacy. Finally, we believe there are approximately an additional 35,000 patients in our target countries, including approximately 15,000 in the United States, who have an elevated ALP greater than ULN but less than 1.67 times ULN who may be treated with Ocaliva.

Our estimates of the potential market opportunity for OCA for the treatment of PBC include a number of key assumptions related to prevalence rates, patients' access to healthcare, diagnosis rates and patients' response to or tolerance of OCA, 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.

Clinical Development Status

As part of our lifecycle management strategy for OCA, we are pursuing the clinical development of Ocaliva as a potential treatment for NASH, PSC and biliary atresia.

Nonalcoholic Steatohepatitis (NASH)

Overview of NASH

NASH is a common and progressive chronic liver disease caused by excessive fat accumulation in the liver, or steatosis, that induces inflammation and may lead to progressive fibrosis and cirrhosis, which may eventually result in liver failure and death. In NASH patients, for reasons that are not yet completely understood, steatosis and other factors such as insulin resistance induce chronic inflammation in the liver and may lead to progressive fibrosis and cirrhosis, followed by eventual liver failure 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. Owing to the rapidly increasing prevalence of the disease, NASH has become the second most common reason for liver transplant in the United States and is projected to become the leading indication for transplant in the next few years, overtaking both chronic hepatitis C infection and alcoholic liver disease. Additionally, NASH is now considered to be the leading, and a rapidly increasing, cause of hepatocellular carcinoma, or 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. More than 30% of those patients are believed to 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 is based on 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, several imaging and circulating biomarkers are being investigated as non-invasive diagnostic methods, including transient elastography (an ultrasound technology approved in Europe and more recently in the United States 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.

Currently Available Treatment Options for NASH

There are currently no drugs 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 ursodiol. 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.

NASH Unmet Medical Need

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.

Breakthrough Therapy Designation

In January 2015, OCA received breakthrough therapy designation from the FDA for the treatment of NASH patients with liver fibrosis. The breakthrough therapy designation was created by the FDA to speed the availability of new therapies for serious or life-threatening conditions. Drugs qualifying for this designation must show credible evidence of a substantial improvement on a clinically significant endpoint over available therapies, or over placebo if there is no available therapy. The breakthrough therapy designation constitutes one of four expedited programs for serious conditions including accelerated approval, priority review and fast-track designation, all of which can also be granted to the same drug if relevant criteria are met. The breakthrough therapy designation confers several benefits, including intensive FDA guidance and discussion and eligibility for submission of a rolling new drug application, or NDA.

Current Status of Clinical Trials

We have conducted or are conducting various clinical trials for the treatment of NASH, including clinical trials required in order to successfully obtain an NDA.

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 through potential amelioration or reversal of liver fibrosis, inflammation, steatosis, and insulin resistance. This is supported by preclinical and clinical results obtained to date, and further investigated in our ongoing clinical trial program. For example, in animal models, sustained FXR activation with OCA treatment has resulted in the reversal of liver fibrosis, the reversal of portal hypertension, the prevention of atherosclerosis, and improvements in triglycerides, inflammation, steatosis and insulin sensitivity. Mice that lack functional FXR (so-called knockout mice) spontaneously develop NASH accompanied by hypertriglyceridemia and insulin resistance, and go on to develop hepatocellular carcinoma, or primary liver cancer. We believe that the combined mechanisms of FXR activation, coupled with the occurrence of NASH in animals lacking FXR, support the potential disease-modifying therapeutic potential of OCA in directly addressing the underlying disease pathology in NASH.

(a) Phase 2 Trial in Type 2 Diabetic Patients with NAFLD

We previously completed 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 gamma-glutamyl transferase, or GGT, and aspartate transaminase, or 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 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-C and slightly decreased concentrations of HDL-C from baseline. In our publication of the results, we observed that once-daily treatment for six weeks at the 25 mg OCA 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.

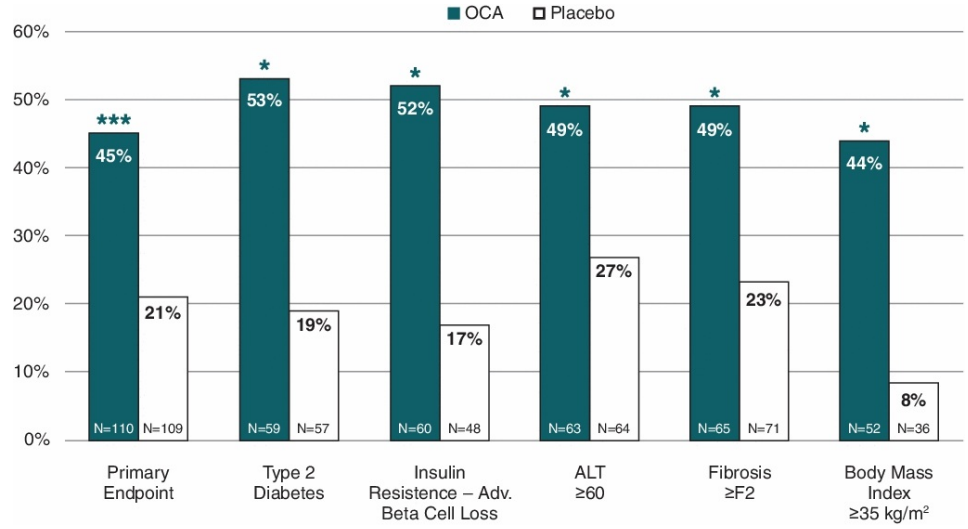
(b) Phase 2 FLINT Trial for NASH

OCA achieved the primary endpoint in a Phase 2b clinical trial for the treatment of NASH, known as the FLINT trial, which was sponsored by the U.S. National Institute of Diabetes and Digestive and Kidney Diseases, or NIDDK, a part of the National Institutes of Health. A significantly greater number of OCA-treated patients also achieved an improvement of at least one fibrosis stage (35% vs 19%, $p = 0.004$), with OCA showing greater response rates as compared to placebo across all stages of fibrosis. The results from the FLINT trial were published in the Lancet in November 2014. This trial was a double-blind, placebo-controlled trial of a once-daily dose of 25 mg of OCA or placebo given for 72 weeks in 283 patients with biopsy-proven NASH.

(i) Primary Endpoint

The percentage of patients meeting the FLINT primary histological endpoint, based on liver biopsies, was defined as a decrease in the NAFLD Activity Score, or NAS, of at least two points with no increase in the fibrosis score following 72 weeks of treatment, 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 hepatocellular ballooning 0 – 2, lobular inflammation 0 – 3 and steatosis 0 – 3). 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, alanine transaminase, or 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). The graph below shows the results of the primary endpoint in the FLINT trial and the improvements in NAS for various subgroups published in the *Lancet*.

Primary Endpoint: Improvement in NAS by ≥ Two Points with no Worsening of Fibrosis



* *p < 0.05, *** p < 0.001. P-values calculated with the Cochran-Mantel-Haenszel test, stratified by clinic and diabetes status.*

(ii) Secondary Efficacy Endpoint: Fibrosis Improvement

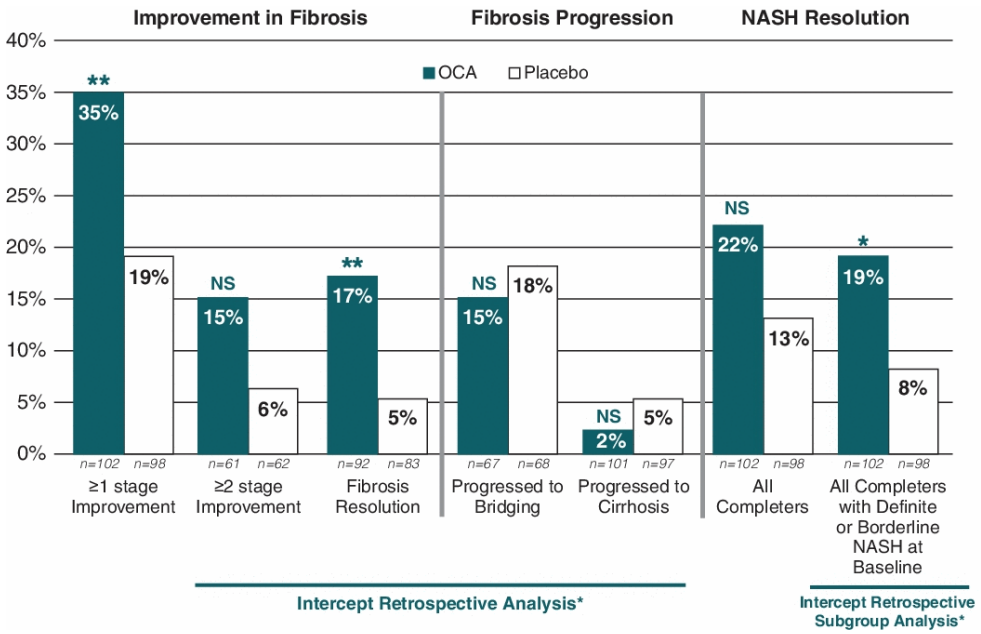
A significantly greater number of OCA-treated patients also achieved an improvement of at least one fibrosis stage (35% versus 19%, p = 0.004). Based on our retrospective analyses of the FLINT data, more OCA-treated patients exhibited fibrosis improvement of at least two fibrosis stages (15% versus 6%, 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). 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.

(iii) Secondary Efficacy Endpoint: NASH Resolution

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, not significant). 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).

The graph below shows these results from the FLINT trial for fibrosis improvement, fibrosis resolution, fibrosis progression and NASH resolution.

FLINT Trial: Improvement in Histological Endpoints



* *p < 0.05, ** p < 0.01. P-values calculated with the Cochran-Mantel-Haenszel test, stratified by clinic and diabetes status. NS indicates that the results are not significant.*

Retrospective analyses after the unblinding of results can potentially introduce bias and regulatory authorities typically give greatest weight to results from pre-specified analyses as compared to retrospective analyses.

(iv) Additional Secondary Endpoints

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 significant reductions in relevant biochemical parameters, including the serum liver enzymes ALT (p < 0.0001), AST (p = 0.0001) and 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 alkaline phosphatase, or 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 average increases in total cholesterol and LDL-C and an average decrease in HDL-C, that developed within 12 weeks of treatment initiation, then began reversing 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 generally 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-C (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-C (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).

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-C 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-C 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-C increase of 8.7 mg/dL at 72 weeks. Patients not treated with statins during the study ($n = 65$) experienced a mean LDL-C increase of 16.0 mg/dL. Treatment related LDL-C increases in all groups reversed with treatment discontinuation. This analysis suggests that the OCA-associated LDL-C 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-C 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 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 above, 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.

(v) Safety and Tolerability

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 in the OCA treatment group occurred more frequently (23% versus 6%, $p < 0.0001$), at a higher grade (predominantly 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. As previously disclosed, two deaths occurred in the OCA treatment group, but neither was considered related to OCA treatment.

(c) Phase 2 Sumitomo Dainippon Trial for NASH

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. In this trial, 202 Japanese biopsy-proven NASH patients (NAS of 5-8) were randomized into one of four arms to receive either a 10mg, 20mg or 40mg 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 intention to treat, or 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, 10 mg, 20 mg and 40 mg OCA groups, respectively).

This 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, not significant). The 40 mg OCA dose group achieved statistical significance on the primary endpoint compared to placebo (p = 0.0496). Dose-dependent trends not reaching statistical significance were also 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	10 mg N = 50	20 mg N = 50	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 CMH (Cochran-Mantel-Haenszel) 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 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, 10 mg, 20 mg and 40 mg OCA groups, respectively. Changes in lipid parameters, including LDL-C, HDL-C 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.

(d) Phase 2 CONTROL Trial

In December 2015, we initiated the 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 two-year long-term safety extension phase.

At the end of the 16-week double-blind treatment period, the CONTROL trial met its primary endpoint in July 2017 by showing that newly initiated treatment with atorvastatin rapidly reversed OCA-associated increases in LDL 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.

During the long-term safety extension phase of CONTROL, there has been one patient death. The principal investigator determined that the events leading to the patient's death were unlikely related to OCA.

(e) Phase 3 REGENERATE Trial

We are currently conducting a Phase 3 clinical trial in non-cirrhotic NASH patients with liver fibrosis, known as the REGENERATE trial.

The REGENERATE trial was designed following discussions with the FDA and EMA. The study population is expected to primarily be comprised of Western NASH patients with histologic evidence of stage 2 or stage 3 liver fibrosis. In addition, the trial will include an exploratory cohort of NASH patients with histologic evidence of early stage 1 liver fibrosis and concomitant diabetes, obesity or elevated ALT, who are at increased risk of disease progression to cirrhosis. These patients with early stage 1 liver fibrosis will not be included in the primary endpoint analysis.

REGENERATE is designed as a double-blind, placebo-controlled Phase 3 clinical trial and is expected to enroll approximately 2,000 NASH patients at more than 350 qualified study sites worldwide and assess the potential benefits of OCA treatment on liver-related and other clinical outcomes. Patients are being randomized into one of three groups receiving a once-daily dose of placebo, 10 mg OCA or 25 mg OCA.

REGENERATE includes a pre-planned interim histology analysis after 72 weeks of treatment in patients with stage 2 or 3 liver fibrosis. If successful, the interim analysis for REGENERATE is intended to serve as the basis for seeking initial U.S. and international marketing approvals of OCA for the treatment of NASH patients with liver fibrosis. The REGENERATE trial will remain blinded after the interim analysis and 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.

In February 2017, we announced modifications to the REGENERATE trial primary endpoint. Based on discussions with the FDA, the primary endpoint for the interim analysis for REGENERATE may be achieved based on one of: (i) the proportion of OCA-treated patients relative to placebo achieving at least one stage of liver fibrosis improvement with no worsening of NASH (defined as no increase in hepatocellular ballooning or lobular inflammation) or (ii) the proportion of OCA-treated patients relative to placebo achieving NASH resolution with no worsening of liver fibrosis. Prior to this modification of the interim analysis, each of the two endpoints was required to be achieved as a co-primary endpoint. Furthermore, we selected a definition for NASH resolution for the trial, which defines a responder as a patient achieving a histologic score of 0 for ballooning and 0 or 1 for inflammation.

As a result of these changes, we anticipate that the interim analysis cohort for REGENERATE will consist of approximately 750 NASH patients with stage 2 or 3 fibrosis. In May 2017, we completed enrollment of the interim analysis cohort for the REGENERATE trial and we anticipate top-line results from the interim analysis in the first half of 2019. We currently intend to seek initial U.S. and international marketing approvals of OCA for the treatment of NASH patients with liver fibrosis based on the interim results from our REGENERATE trial.

In a retrospective analysis of data from the FLINT trial conducted in a REGENERATE-matched patient cohort, approximately 43% 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=0.0059). In a similar retrospective analysis on the FLINT data using the definition we selected for NASH resolution, approximately 20% of OCA-treated patients, as compared to approximately 6% of patients on placebo achieved NASH resolution with no worsening of fibrosis (p = 0.0289).

(f) Phase 3 REVERSE Trial

We have initiated a Phase 3 trial in NASH patients with cirrhosis, known as the REVERSE trial. REVERSE is a randomized, double-blind, placebo-controlled, multi-center study to evaluate the efficacy and safety of OCA in approximately 540 patients with a biopsy-confirmed diagnosis of cirrhosis due to NASH.

The primary endpoint of the study is the percentage of subjects with histological improvement in fibrosis by at least one stage using the NASH Clinical Research Network scoring system after 12 months of treatment. Patients are being randomized in a 1:1:1 ratio to one of the three treatment arms: once-daily dosing of OCA 10 mg, once-daily OCA 10 mg with titration to 25 mg at three months, or placebo. 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.

Primary Sclerosing Cholangitis (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 and its complications.

PSC is usually diagnosed by preliminary assessment of liver biochemistry, with or without reported symptoms, and confirmed by cholangiography, typically magnetic resonance cholangiopancreatography or endoscopic retrograde cholangiopancreatography, or ERCP. 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 previously estimated as 8 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, liver transplant is currently the only treatment shown to improve clinical outcomes. Ursodiol is often used for the treatment of PSC due to improvements in liver biochemistry following initiation of therapy. Despite general biochemical improvement, ursodiol has not been shown to improve transplant-free survival and, at high doses, has been associated with increased risk for serious complications. However, as there are no approved drugs for the treatment of PSC, some physicians treat patients with ursodiol, typically at a dose of 13 to 15 mg/kg/day. PSC is the fourth leading indication for liver transplant. However, the post-transplant recurrence rate of PSC has been shown to be as high as 20%.

Phase 2 AESOP Trial: OCA as Therapy in PSC

In July 2017, we announced top-line 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. The primary endpoint was the reduction of serum ALP levels, as compared to placebo. 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. In October 2017, additional results from the AESOP trial were presented. OCA achieved the primary endpoint of the AESOP trial: patients receiving 5 mg of OCA 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 were randomized to one of three treatment groups: placebo, OCA 1.5 – 3 mg and OCA 5 – 10 mg (with dose titration occurring at the 12-week midpoint).

(U/L)	Placebo (N = 25)	OCA 1.5 – 3 mg (N = 25)	OCA 5 – 10 mg (N = 26)
Mean Baseline ALP	563	423	429
Least Squares (LS) Mean Change from Baseline in ALP at Week 12	-53	-57	-135*
LS Mean Change from Baseline in ALP at Week 24	-27	-105	-110*†
LS Mean Percent Change from Baseline at Week 24	+1%	-22%*	-22%*

* $p < 0.05$

† Primary endpoint was ALP change for OCA 5 – 10 mg compared to placebo at week 24.

Patients in the OCA 1.5 – 3 mg group achieved statistically significant reductions in ALP versus placebo as measured by least square, or 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 – 3 mg and OCA 5 – 10 mg groups ($p < 0.05$).

In AESOP, a significant proportion of patients used ursodiol, with 48%, 48% and 46% of patients on placebo, OCA 1.5 – 3 mg and OCA 5 – 10 mg, respectively, receiving ursodiol at baseline. In a post-hoc analysis examining the effects of OCA in the presence and absence of ursodiol, ALP reductions were observed with OCA regardless of treatment with ursodiol. 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 ursodiol. At week 12, patients in the OCA 5 – 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 ursodiol. At week 24, LS mean reductions in ALP in the OCA 5 – 10 mg group were 25% for patients receiving OCA monotherapy and 14% for patients receiving OCA in combination with ursodiol.

Pruritus is a common symptom of PSC and was the most common adverse event observed in AESOP, occurring in 46%, 60% and 67% of patients in the placebo, OCA 1.5 – 3 mg and OCA 5 – 10 mg groups, respectively.

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.

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.

Phase 2 CARE Trial: OCA as Therapy in Biliary Atresia

In October 2015, we initiated a Phase 2 clinical trial of OCA, known as the CARE trial, in pediatric patients with biliary atresia. The CARE trial will 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 anticipated to enroll approximately 60 patients in the United States and Europe. In addition to studying the effects of OCA treatment in biliary atresia, this trial is a part of the approved Pediatric Investigation Plan, or PIP, in support of the Marketing Authorization Application, or MAA, for OCA in PBC in the European Union.

Potential Future Product Candidates

In addition to OCA, we are developing other novel bile acid analogs targeting FXR and a second dedicated bile acid receptor called TGR5, which is a target of particular interest for the treatment of type 2 diabetes and other gastrointestinal indications. In order to streamline operating expenses, we plan to deprioritize our development programs in these products for the foreseeable future.

INT-767

INT-767 is an orally administered dual FXR and TGR5 agonist that, like OCA, is derived from the primary human bile acid chenodeoxycholic acid, or CDCA. This product candidate has been shown to be approximately three times more potent than OCA as an FXR agonist. In animal models of chronic liver, intestinal and kidney diseases, INT-767 has consistently demonstrated greater anti-fibrotic and anti-inflammatory effects than OCA.

We have received assignments of rights to the INT-767 patent portfolio from all inventors, with the exception of one inventor. That inventor is contractually obligated to provide an assignment to us. Thus, we believe that we are the owner of the INT-767 patent portfolio by virtue of this contractual obligation and the patent assignments we have received.

We have completed a Phase 1 clinical trial of INT-767 in healthy volunteers. The goal of the Phase 1 trial was to assess safety and pharmacokinetics in a single ascending dose escalation phase followed by a multiple ascending dose phase in healthy volunteers.

INT-777

INT-777 is an orally administered TGR5 agonist that is derived from the primary human bile acid cholic acid. We have completed preclinical studies necessary for the filing of an IND. By virtue of the patent assignments we have received and other contractual obligations owed to us, we believe we are the exclusive owner of the INT-777 patent portfolio.

Our in vitro studies of INT-777 showed that the product candidate has the potential to selectively target TGR5, a receptor that has been shown to directly regulate the release of glucagon like peptide-1, or GLP-1, a gastrointestinal peptide hormone with potent anti-diabetic effects. TGR5 has also been shown in animal models to regulate other metabolic pathways in brown fat and skeletal muscle that drive energy expenditure. The receptor may also play a role in the control of inflammation, which is increased in insulin resistant diabetic conditions.

In animal models of diabetes, treatment with INT-777 induced GLP-1 secretion, with resulting insulin sensitivity and normalization of glycemic control, increased basal energy expenditure and prevention of weight gain, and a reduction in blood lipid levels together with liver steatosis and fibrosis. We believe that these preclinical results could support further development of INT-777 and our other TGR5 agonists in the treatment of type 2 diabetes, associated metabolic disorders and other gastrointestinal indications.

Strategic Collaborations and Research Arrangements

Sumitomo Dainippon Pharma

On March 29, 2011, we entered into a license agreement with Sumitomo Dainippon, under which we granted Sumitomo Dainippon an exclusive license to research, develop and commercialize OCA as a therapeutic for the treatment of PBC and NASH in Japan and China (excluding Taiwan). Under the terms of the agreement, Sumitomo Dainippon is required to use commercially reasonable efforts to develop and commercialize OCA in its licensed territories for the treatment of PBC and NASH, and we are obligated under the agreement to use commercially reasonable efforts to develop OCA outside of Sumitomo Dainippon's licensed territories. We are also responsible for supplying Sumitomo Dainippon with a clinical and commercial supply of OCA requested by Sumitomo Dainippon pursuant to clinical and commercial supply agreements that include terms specified in the agreement. Sumitomo Dainippon has agreed, during the term of the agreement, to not commercialize any compound that is an FXR agonist for use in the treatment of PBC or NASH other than pursuant to the agreement.

We granted Sumitomo Dainippon an option under the agreement to obtain an exclusive license to commercialize OCA for indications other than PBC and NASH on the same terms as are set forth in the agreement. Sumitomo Dainippon may exercise this option with respect to any indication at any time during the two-year period commencing on the date we notify Sumitomo Dainippon of the commencement of a Phase 3 clinical trial involving OCA for such indication, subject to Sumitomo Dainippon's payment of an option fee for each additional indication. No option fee is required to be paid by Sumitomo Dainippon if it exercises its option for any additional indication in China.

In addition to Japan and China, which are the original licensed territories, we also granted Sumitomo Dainippon an option under the agreement to add Korea, Taiwan, Malaysia, Vietnam, the Philippines, Thailand, Singapore and/or Indonesia to its exclusive license on the same terms as are set forth in the agreement (the "Country Option"). In May 2014, Sumitomo Dainippon exercised its option to add Korea to its licensed territories.

In February 2018, we amended our license agreement with Sumitomo Dainippon. Under the amendment, Sumitomo Dainippon agreed to return the rights to develop and commercialize OCA in Japan and Korea and we agreed to forego any further milestone or royalty payments for the development and commercialization of OCA in such countries. In addition, Sumitomo Dainippon waived its rights to the Country Option and the parties adjusted certain milestone payment obligations with respect to the development and commercialization of OCA.

Sumitomo Dainippon may be required to pay us up to an aggregate of approximately $4 million for the achievement of development milestones, $19 million for the achievement of regulatory approval milestones and tiered royalties up to the mid-twenties in percentage terms based on net sales of OCA products in China. The term of the agreement, and Sumitomo Dainippon's obligation to pay royalties to us for each OCA product, expires in China on the later of the expiration of the exclusivity period in China, whether through the expiration of applicable patents or the introduction of generic drugs that compete with the OCA product, or ten years after the first commercial sale of such OCA product for the first or second indication in China. Under the amendment, the parties also agreed that if certain clinical development milestones in China are not met by December 31, 2020, Sumitomo Dainippon may choose either to pay the Company a milestone payment or terminate the Agreement.

Royalty rates are subject to reduction under the agreement in specified circumstances, including if sales of generic products reach a certain threshold market share in China over a specified period.

Sumitomo Dainippon may terminate the agreement in its entirety, with respect to China or on an indication-by-indication basis upon 90 days' written notice. Either we or Sumitomo Dainippon may terminate the agreement in the event of the uncured material breach by or bankruptcy of the other party, subject to certain dispute resolution procedures. If Sumitomo Dainippon were to terminate the agreement for our material breach, it would have a perpetual license following the effective date of termination, subject to the payment by Sumitomo Dainippon of a royalty based on net sales of OCA products, the amount of which will depend on whether the effective date of termination occurs prior to or after the date of first commercial sale of an OCA product. If we were to terminate the agreement for Sumitomo Dainippon's material breach or if Sumitomo Dainippon were to voluntarily terminate the agreement, Sumitomo Dainippon's license under the agreement would terminate.

Competition

The biopharmaceutical industry is characterized by intense competition and rapid innovation. Our potential competitors include major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies and universities and other research institutions. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. We believe the key competitive factors that will affect the development and commercial success of our product candidates are efficacy, safety and tolerability profile, reliability, convenience of dosing, price, the level of generic competition and reimbursement.

We compete, and will continue to compete, with existing and new products being developed by our competitors. Some of these competitors are pursuing the development of pharmaceuticals that target the same disease and conditions that our research and development programs target.

For example, Ocaliva competes with ursodiol, a first line therapy that is approved for treatment and is generically available at a significantly lower cost than branded products.

Ocaliva is an FXR agonist. 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 International AG (LJN452), Gilead Sciences, Inc. (GS-9674) and Enanta Pharmaceuticals, Inc. (EDP-305). Additional product candidates in Phase 2 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 (ADP334), Bristol-Myers Squibb's marketed anti-CTL4 fusion protein (abatacept), and FF Pharmaceuticals' 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 (GSK2330672).

The use of Ocaliva to treat PBC also competes off-label with fibrates. While many fibrates are specifically contraindicated for use in PBC due to potential concerns over acute and long-term safety in this patient population. An investigator-sponsored Phase 3 trial of bezafibrate, a fibrate that has not been approved for commercialization by the FDA only available outside of the United States, has been completed. Dr. Falk Pharma GmbH is running a Phase 3 trial evaluating a combination of ursodiol and budesonide, a steroid.

With respect to NASH, there are currently no therapeutic products approved for the treatment of NASH, NAFLD, portal hypertension, complications of cirrhosis or alcoholic hepatitis. If approved, Ocaliva for the treatment of NASH, would compete with several marketed therapeutics that are currently used off-label for the treatment of NASH, such as vitamin E (an antioxidant), insulin sensitizers (e.g., metformin), antihyperlipidemic agents (e.g., gemfibrozil), pentoxifylline and ursodiol. Additionally, there are ongoing and announced Phase 3 clinical trials by our competitors for the treatment of NASH, including Genfit SA's PPAR alpha/delta agonist (elafibranor), Gilead Sciences, Inc.'s ASK-1 inhibitor (GS-4997) and Allergan's dual CCR2 and CCR5 inhibitor (cenicriviroc), as well as several FXR agonists in Phase 2 or earlier clinical or preclinical development for the treatment of NASH, including, FXR agonists from Novartis International AG (LJN452), Gilead Sciences, Inc. (GS-9674) and Enanta Pharmaceuticals, Inc. (EDP-305).

Additional product candidates in Phase 2 or earlier clinical or preclinical development for the treatment of NASH include Bristol-Myers Squibb Co., Novo Nordisk A/S, Conatus Pharmaceuticals Inc., Cymabay Therapeutics, Inc., Islet Sciences, Inc., Galectin Therapeutics Inc., Zydus Pharmaceuticals Inc., NGM Biopharmaceuticals Inc., Galmed Medical Research Ltd., MediciNova, Inc., Ionis Pharmaceuticals, Inc., FibroGen, Inc., Viking Therapeutics, Inc., AstraZeneca plc, Durect Corporation, Immuron Ltd., Boehringer Ingelheim GmbH, MiNA Therapeutics, NuSirt Biopharma, Inc., Protalix Biotherapeutics, and Medivation, Inc.

With respect to PSC, there is no approved treatment for PSC. If approved, Ocaliva, for the treatment of PSC, would compete off-label with ursodiol. We are also aware of several companies that have product candidates in Phase 2 clinical or earlier stage preclinical development for the treatment of PSC, including Allergan Plc, Biotie Therapies Corp. (acquired by Acorda Therapeutics, Inc.), Dr. Falk Pharma GmbH, Durect Corporation, Gilead Sciences, Inc. and Shire plc.

We believe that OCA offers key potential competitive advantages over ursodiol and other products in development. However, many of our potential competitors have substantially greater financial, technical and human resources than we do, as well as greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Accordingly, our competitors may be more successful than us in obtaining approval from the FDA or from other regulators for drugs and achieving widespread market acceptance. Our competitors' drugs may be more effective, or more effectively marketed and sold, than any product candidate we may commercialize and may render our product candidates obsolete or non-competitive before we can recover the expenses of their development and commercialization. We anticipate that we will face intense and increasing competition as new drugs enter the market and other advanced technologies become available. Finally, the development of new treatment methods for the diseases we are targeting could render our product candidates non-competitive or obsolete. NASH is a complex disease and it is unlikely that any one therapeutic option will be optimal for every NASH patient. In addition, our ability to compete may be affected because, in many cases, insurers or other third-party payors seek to encourage the use of generic products.

Intellectual Property

The proprietary nature of, and protection for, our product candidates and our discovery programs, processes and know-how are important to our business. We have sought patent protection in the United States and internationally for OCA, INT-767 and INT-777, and our discovery programs, and other inventions to which we have rights, where available and when appropriate. Our policy is to pursue, maintain and defend patent rights, whether developed internally or licensed from third parties, and to protect the technology, inventions and improvements that are commercially important to the development of our business. We also rely on trade secrets that may be important to the development of our business.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection of our current and future product candidates and the methods used to develop and manufacture them, as well as successfully defending these patents against third-party challenges. Our ability to stop third parties from making, using, selling, offering to sell or importing our products depends on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our product

candidates, discovery programs and processes. For this and more comprehensive risks related to our intellectual property, please see Item 1.A. "Risk Factors — Risks Related to Our Intellectual Property."

OCA (lead product candidate; FXR agonist)

The patent portfolio for OCA contains patents and patent applications directed to compositions of matter, manufacturing methods, and methods of use. As of December 31, 2017, we owned eleven U.S. patents, thirteen pending U.S. patent applications, and corresponding foreign patents and patent applications. Foreign patents have been granted in 30 European countries as well as Australia, Canada, China, India, Israel, Japan, and Macao. We expect the composition of matter patents, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire in 2022 (worldwide) at the soonest and 2033 at the latest. In conjunction with the accelerated approval of Ocaliva in the United States, we have applied to extend the 2022 expiration date of the composition of matter patent in the United States by five additional years under the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act. We have also made a similar application in Europe in conjunction with the conditional approval of Ocaliva for a supplementary protection certificate to extend the composition of matter patent in Europe by five additional years. Patent term extension may be available in certain foreign countries upon regulatory approval. We expect the other patents in the portfolio, if the appropriate maintenance, renewal, annuity, or other governmental fees are paid, to expire from 2022 to 2033.

INT-767 (dual FXR/TGR5 agonist)

The patent portfolio for INT-767 contains patents and patent applications directed to compositions of matter and methods of use. As of December 31, 2017, we owned five U.S. patents, seven pending U.S. patent applications, and corresponding foreign patents and patent applications. Foreign patents have been granted in Australia, Canada, China, 32 European countries as well as Hong Kong, India, Israel and Japan. We expect the issued composition of matter patent in the United States, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire in 2029. It is possible that the term of the composition of matter patent in the United States may be extended up to five additional years under the provisions of the Hatch-Waxman Act. We expect the foreign composition of matter patents, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire in 2027. Patent term extension may be available in certain foreign countries upon regulatory approval. We expect the other patents in the portfolio, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire from 2027 to 2029.

INT-777 (TGR5 agonist)

The patent portfolio for INT-777 contains patents and patent applications directed to compositions of matter and methods of use. As of December 31, 2017, we owned five U.S. patents, one pending U.S. patent applications, and corresponding foreign patents and patent applications. Foreign patents have been granted in Australia, China, 9 Eurasian countries, 30 European countries, Hong Kong, Israel, Japan, Macao, Mexico, Singapore, South Korea, and South Africa. We expect the composition of matter patent in the United States, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire in 2030. It is possible that the term of the composition of matter patent in the United States may be extended up to five additional years under the provisions of the Hatch-Waxman Act. We expect the foreign composition of matter patents, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire beginning in 2028. Patent term extension may be available in certain foreign countries upon regulatory approval. We expect the other patents in the portfolio, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire from 2028 to 2030.

Trade Secrets

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. Trade secrets and know-how can be difficult to protect. We seek to protect our proprietary processes, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and commercial partners. These agreements are designed to protect our 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.

Manufacturing

We do not own or operate manufacturing facilities for the production of Ocaliva or any of our product candidates, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We currently rely on third-party contract manufacturers for all of our required raw materials, active pharmaceutical ingredient, or API, and finished product for commercial sales and for our clinical trials and preclinical studies.

We currently have a commercial manufacturing and supply agreement with PharmaZell GMBH, or PharmaZell that we entered into in September 2016. Under the agreement we have agreed to purchase from PharmaZell a certain percentage of our annual commercial requirements of API for use in Ocaliva. We also agreed to purchase specified minimum quantities of API. The agreement is effective until December 31, 2020, subject to two-year automatic renewal terms, unless either party provides notice of non-renewal at least 12 months prior to the end of the initial term or the then-current renewal term. We may terminate the agreement immediately with written notice upon the occurrence of certain regulatory events, or if PharmaZell fails to meet certain quality standards, applicable laws or specified delivery obligations. Each party also has the right to terminate the Agreement immediately upon written notice for other customary reasons such as material breach and bankruptcy.

We are currently seeking to qualify one or more back-up API manufacturers and we do not have any current contractual relationships for the manufacture of commercial supplies of any of our products or product candidates other than OCA. We currently obtain these supplies and services from our third-party contract manufacturers on a purchase order basis. We intend to enter into agreements with a third-party contract manufacturer and one or more back-up manufacturers for the commercial production of those product candidates.

Contract manufacturers are subject to extensive governmental regulation and we depend on them to manufacture Ocaliva and our product candidates in accordance with applicable current good manufacturing practice regulations or cGMPs. Development and commercial quantities of any products that we develop will need to be manufactured in facilities, and by processes, that comply with the requirements of the FDA, EMA and the regulatory agencies of other jurisdictions in which we are seeking approval.

Sales and Marketing

We are commercializing Ocaliva in the United States, Europe and Canada using our internal commercial organization, as well as a contract sales organization. We have built and plan to continue to expand our commercial infrastructure in Europe, Canada and Australia and will likely seek to commercialize OCA through distribution or other collaboration arrangements outside of the United States, Europe, Canada and Australia, subject to obtaining necessary marketing approvals. We also have a team of field-based medical science liaisons, who play an important role in providing medical information about Ocaliva to clinicians and other health care professionals.

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, or 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, or GLP, regulations;
- submission to the FDA of an investigational new drug, or IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or 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, or 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, or 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 Risk Evaluation and Mitigation Strategies, or REMS, and post-approval studies required by the FDA.

Preclinical 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 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, or 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. Disclosure of the results of these clinical trials can be delayed until the product or new indication being studied has been approved. 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, or 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 will be binding on the FDA and 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.

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 or a supplemental 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 $2.4 million for NDAs with clinical information and approximately $1.2 million for supplemental NDAs without clinical information. The manufacturer and/or sponsor under an approved NDA is also subject to annual product and establishment user fees, currently $304,162. 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 are 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. 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 th 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, or IMM, 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 ursodiol. 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.

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 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 accordance 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. Finally, we have also 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, or FDAAA, 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, referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits an extension 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. In conjunction with the accelerated approval of Ocaliva in the United States, we have applied to extend the 2022 expiration date of the OCA composition of matter patent in the United States by five additional years under the provisions of the Hatch-Waxman Act. We have also applied to extend the 2022 expiration date of the OCA composition of matter patent in Europe by five additional years (known as Supplementary Patent Certification, or "SPC"). 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. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. 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 for drugs containing the original active agent 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, or BPCA, certain drugs may obtain an additional six months of exclusivity, 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, or PREA, an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, 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 where there is a demonstration of clinical superiority. Orphan drug exclusivity, however, could also block the approval of one of our products for seven years if a competitor obtains approval of the same drug as defined by the FDA or if our drug candidate is determined to be the same drug as a drug in competitor's product for the same indication or disease. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. 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 exclusivity.

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. Any of our orphan-designated products and product candidates can lose orphan designation, and the related benefits, if it is demonstrated that the orphan designation criteria are no longer met. In addition, some lawmakers in the US have expressed concern about whether the Orphan Drug Act should be reformed based on a concern that it has incentivized a rise in prescription drug costs.

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 a 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 by the EMA's Committee for Human Medicinal Products for Human Use (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, 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 marketing authorization from the EMA could be conditional on post-approval studies and not considered a full approval. 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 Committee for Medicinal Products for Human Use, or 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 does not 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 health 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 of 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. If these third-party payors do not consider our products to be effective (or cost-effective in some markets outside of the United States) compared to other therapies, they may not cover our products after they are approved as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to 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 will provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Part D prescription drug plan sponsors are not required to pay for all covered 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 drugs within each therapeutic category and class of covered 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 therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D plan will likely be lower than the prices we might otherwise obtain. 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 payment made by Medicare may result in a similar reduction in payments from non-governmental payors.

Medicaid is a government 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 with 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 Rebate Agreement to have its products be eligible for coverage by Medicaid. Under the Medicaid program, and per the Medicaid 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 January 2016, the Centers for Medicare & Medicaid Services, or CMS, released a final rule impacting the calculation and reporting of prices by manufacturers under the Medicaid program. We continue to evaluate how this final rule may affect the reimbursement of our product candidate and rebates paid to state Medicaid programs.

Federal law requires any company that participates in the Medicaid Drug Rebate Program to also participate in the Public Health Service's 340B drug pricing program in order for federal funds to be available for the manufacturer's drugs under Medicaid. The 340B 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, or, collectively, the ACA, extended eligibility to participate in the 340B pricing 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.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, ACA, became law in the United States. Among other things, the ACA was enacted to reduce the cost of health care and substantially change the way health care 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 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 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. There is still uncertainty whether the ACA will undergo additional revisions, and we cannot predict the impact of any future modifications, and it is uncertain how any such proposals, if approved, would affect these provisions. 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, including a 2017 California law, currently being challenged, that would require manufacturers to provide advanced notification of price increases to certain purchasers and report specified drug pricing information to the state We cannot predict the success of current or future federal or state legislative efforts.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research will be developed by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of any product, if any such product or the condition that it is intended to treat is the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of our product candidates. If third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

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 other 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 and formulary managers, 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.

Other Laws

The Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or, collectively, HIPAA, imposes criminal liability for executing a scheme to defraud any healthcare benefit program. and for knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services. HIPAA also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. 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 Department of Health and Human Services information related to payments and other transfers of value made to covered recipients, such as physicians and teaching hospitals, and physician ownership and investment interests. 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 various EU countries where we have operations.

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.

Employees

As of December 31, 2017, we had 507 employees, including 158 in research and development, 172 in our commercial organization, 75 in our medical affairs group and 102 in general and administrative supporting functions. Geographically, 340 of our employees were based in the United States and 167 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 Information

We were incorporated in the State of Delaware on September 4, 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 also have administrative offices in San Diego, California and London, United Kingdom.

Our corporate website address is *www.interceptpharma.com.* Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to reports filed pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, are available free of charge on our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission. The Securities and Exchange Commission maintains an internet site that contains our public filings with the Securities and Exchange Commission and other information regarding our company at *www.sec.gov.* These reports and other information concerning the Company may also be accessed at the Securities and Exchange Commission's Public Reference Room at 100 F Street, NE, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the Securities and Exchange Commission at 1-800-SEC-0330. The contents of these websites are not incorporated into this Annual Report. Further, our references to the URLs for these websites are intended to be inactive textual reference only.

Legal Proceedings

The Company is involved in various legal proceedings in the normal course of its business, including intellectual property litigation, employment litigation and other litigation. The outcome of such litigation is uncertain, and the Company may from time to time enter into settlements to resolve such litigation. The following discussion is limited to the Company's material on-going legal proceedings:

On August 4, 2017, a derivative lawsuit purportedly brought on behalf of Intercept, styled Solak v. Fundaro, et al, was filed in the Supreme Court of the State of New York, County of New York. This lawsuit was filed by a purported stockholder of the Company, and purports to assert derivative claims on behalf of the Company against Intercept's directors for breach of fiduciary duty, waste and unjust enrichment arising out of the Company's non-executive director compensation practices. The lawsuit seeks money damages; an order directing the Company to take all necessary actions to reform and improve its corporate governance and internal procedures relating to non-employee director compensation; equitable and injunctive relief, including by restricting the proceeds of the defendants' trading activities or other activities to ensure that the plaintiff has an effective remedy; restitution from the defendants; and costs and fees.

On September 25, 2017, the defendants moved to dismiss the action. Following briefing on the defendants' motion to dismiss, oral argument was held on December 5, 2017. A decision has not been rendered on the motion.

On September 27, 2017, a purported shareholder class action, styled Judith DeSmet v. Intercept Pharmaceuticals, Inc., Mark Pruzanski and Sandip S. Kapadia was filed in the United States District Court for the Southern District of New York, naming us and certain of our officers as defendants. This lawsuit was filed by a stockholder who claims to be suing on behalf of anyone who purchased or otherwise acquired our securities between May 31, 2016 and September 20, 2017. The lawsuit alleges that we made material misrepresentations and/or omissions of material fact in our public disclosures during the period from May 31,

2016 and September 20, 2017, in violation of Sections 10(b) and 20(a) of the Exchange Act and Rule 10b-5 promulgated thereunder. The alleged improper disclosures relate to statements regarding our business, operational and compliance policies. The plaintiff seeks unspecified monetary damages on behalf of the putative class and an award of costs and expenses, including attorney's fees. On January 5, 2018, a follow-on derivative suit, styled Davis v. Pruzanski et al., was filed in New York state court by shareholder Gregg Davis based on substantially the same allegations as the securities case. On December 1, 2017, a purported shareholder demand was brought based on substantially the same allegations as those set forth in the securities case.

We believe that we have valid defenses to the claims in the lawsuits described above and intend to defend ourselves vigorously. At this time, no assessment can be made as to the likely outcome of these lawsuits or whether the outcome will be material to us. Therefore, we have not accrued for any loss contingencies related to these lawsuits.

Item 1.A. Risk Factors

Except for the historical information contained herein, this Annual Report contains forward-looking statements that involve risks and uncertainties. These statements include projections about our accounting and finances, plans and objectives for the future, future operating and economic performance and other statements regarding future performance. These statements are not guarantees of future performance or events. Our actual results could differ materially from those discussed in this Annual Report. Important factors that could cause or contribute to these differences include, but are not limited to, those discussed in the following section, as well as those discussed in Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere throughout this Annual Report.

You should consider carefully the following risk factors, together with all of the other information included in this Annual Report. If any of the following risks, either alone or taken together, or other risks not presently known to us or that we currently believe to not be significant, develop into actual events, then our business, financial condition, results of operations or prospects could be materially adversely affected. If that happens, the market price of our common stock could decline, and stockholders may lose all or part of their investment.

Risks Related to Our Financial Position and Need for Additional Capital

We are 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 ursodiol in adults with an inadequate response to ursodiol or as monotherapy in adults unable to tolerate ursodiol.

Our ability to generate profits from operations and become profitable will depend on the success of commercial sales of Ocaliva. However, the successful commercialization of Ocaliva in PBC is subject to many risks. We are currently undertaking our first commercial launch with Ocaliva in PBC, and there is no guarantee that we will be able to do so successfully. There are numerous examples of unsuccessful product launches and failures to meet expectations of market potential, including by pharmaceutical companies with more experience and resources than us.

The commercial success of Ocaliva 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 Ocaliva will have in PBC. For example, if the patient population suffering from PBC is smaller than we estimate, or even if the patient population matches our estimate but Ocaliva is not widely accepted as a treatment for PBC, the commercial potential of Ocaliva 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. Furthermore, any negative development in any other development program of 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 adversely impact the commercial results and potential of Ocaliva.

As a result, we cannot foresee if Ocaliva will ever be accepted as a therapy in PBC that eventually results in revenues that can sustain operations. It may take the passage of a significant amount of time to generate sufficient revenues to sustain operations even if Ocaliva becomes accepted as a therapy in PBC. Furthermore, because Ocaliva is still undergoing regulatory review in a number of jurisdictions outside of the United States and the European Union, we may not be able to commercialize Ocaliva in PBC in such other jurisdictions, which may also limit our prospects. If the commercialization of Ocaliva for PBC is unsuccessful or perceived to be disappointing, the long-term prospects of Ocaliva and our company may be significantly harmed.

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 have incurred net losses of $360.4 million, $412.8 million and $226.4 million for the years ended December 31, 2017, 2016 and 2015, 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, 2017, we had $414.9 million in cash, cash equivalents and investment securities.

We have devoted substantially all of our resources to our development efforts relating to our product candidates, including conducting clinical trials of our product candidates, providing general and administrative support for these operations, protecting our intellectual property and engaging in activities to prepare for and commercially launch Ocaliva in PBC.

We expect to continue to incur losses for the foreseeable future, and we expect these losses to increase as we continue to commercialize Ocaliva for PBC in jurisdictions where marketing approval has been received, seek regulatory approval for and prepare to commercially launch Ocaliva for PBC in jurisdictions without marketing approval, develop and seek regulatory approvals for OCA in NASH, and other indications, and add infrastructure and personnel in the United States and internationally to support our product development and commercialization efforts and operations as a public company. 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 and PSC. 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 OCA in PBC, continue our Phase 3 clinical program of OCA in NASH, including the Phase 3 REGENERATE trial in non-cirrhotic NASH patients with liver fibrosis and our Phase 3 REVERSE trial in NASH patients with compensated cirrhosis and continue the development of OCA in PSC. We also expect to continue the development of OCA in additional diseases, such as biliary atresia, a rare pediatric disease characterized by deficient bile duct development for which we initiated a Phase 2 trial in OCA called CARE. Our overall development program for OCA in NASH is expected to include a number of other trials, including clinical trials required to submit an NDA for NASH. 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 regulatory approval, or if they do 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 accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. The amount of future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues.

We will require substantial additional funding, which may not be available to us on acceptable terms, or at all, and, if not so available, may require us to delay, limit, reduce or cease our operations.

We are currently advancing OCA through clinical development for multiple indications and other product candidates through various stages of clinical and preclinical development. Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive.

In addition, subject to obtaining regulatory approval of any of our product candidates, we expect to incur significant commercialization expenses for product sales, marketing, manufacturing and distribution. We have incurred and anticipate incurring significant expenses as we continue to commercialize Ocaliva in PBC. As part of our longer-term strategy, we also anticipate incurring significant expenses in connection with our product development, scientific, commercial and administrative personnel and facilities and infrastructure in the United States and abroad. We also expect to incur additional costs associated with operating as a public company. We may also engage in activities that involve potential in- or out-licensing of products or technologies or acquisitions of other products, technologies or businesses.

As of December 31, 2017, we had $414.9 million in cash, cash equivalents and investment securities. We currently project adjusted operating expenses in the range of $390 million to $410 million in the fiscal year ending December 31, 2018, which excludes stock-based compensation and other non-cash items. These expenses are planned to support the continued commercialization of Ocaliva in PBC in the United States and other markets, and continued clinical development for OCA in PBC and NASH and our other earlier stage pipeline programs. We may make additional investments over 2018 as our business evolves. Accordingly, we will continue to require substantial additional capital in connection with our continuing operations, including continuing our clinical development and commercialization activities, despite having started to generate revenues from product sales. Because successful development and commercialization of our products and product candidates is uncertain, we are unable to estimate the actual funds required to complete the research and development and commercialization of our products and product candidates.

Adjusted operating expense is a financial measure not calculated in accordance with GAAP. We anticipate that stock-based compensation expense will represent the most significant non-cash item that is excluded in adjusted operating expenses as compared to operating expenses under GAAP. See Item 7. “Management’s Discussion and Analysis of Financial Condition and Results of Operation” — “Non-GAAP Financial Measures” for more information.

Due to the many variables inherent to the development and commercialization of novel therapies, such as the risks described in this “Risk Factors” section of this Annual Report, and our rapid growth and expansion, we currently cannot accurately or precisely predict the duration beyond mid-2019 over which we expect our cash and cash equivalents to be sufficient to fund our operating expenses and capital expenditure requirements. However, we currently believe that our cash and cash equivalents will be sufficient for us to:

- continue the initial commercialization of Ocaliva for PBC in the United States, the European Union and other jurisdictions where it has received marketing approval;
- prepare for and initiate the commercial launch of Ocaliva in PBC in certain other target markets across the world, but not commercially launch Ocaliva in PBC in other non-target countries across the world;
- continue and expand our clinical development programs for OCA in PBC and NASH, such as continuing, but not completing, our planned Phase 3 clinical program for OCA in NASH, including the REGENERATE trial and the REVERSE trial, and our ongoing COBALT confirmatory clinical outcomes trial of OCA in PBC; and
- conduct further assessments of OCA for use in PSC and potentially initiate, but not complete, additional clinical trials for OCA in PSC.

Accordingly, we will continue to require substantial additional capital in connection with our continuing operations, including continuing our commercialization plans and our research and development activities and building our global infrastructure to support these activities.

The amount and timing of our future funding requirements will depend on many factors, including:

- the rate of progress and cost of our continued commercialization activities for Ocaliva in PBC in jurisdictions where it has received marketing approval;
- our ability to receive marketing approval of Ocaliva for PBC in countries where it has not received marketing approval based on our regulatory submissions package and our work completed to date, including the willingness of the relevant regulatory authorities to accept the POISE trial, which is our completed Phase 3 clinical trial for PBC;
- the degree of effort and time needed to prepare for and initiate the commercial launches of Ocaliva in PBC in the jurisdictions where it receives marketing approval;
- the progress, costs, results of and timing of our clinical development programs for OCA in PBC, NASH, PSC and other indications, such as the COBALT trial, the REGENERATE trial, the REVERSE trial or other trials we may conduct;

- the outcome, costs and timing of seeking and obtaining FDA, EMA and any other regulatory approvals;
- the expansion of our research and development activities and the product candidates that we pursue, including INT-767 and our product candidates in preclinical development such as INT-777;
- the expansion of our operations, personnel and the size of our company and our need to continue to expand in the longer term;
- the costs associated with securing and establishing manufacturing capabilities and procuring the materials necessary for our products and product candidates;
- market acceptance of our products and product candidates, which may be affected by reimbursement from payors;
- the costs of acquiring, licensing or investing in businesses, products, product candidates and technologies;
- our ability to maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights;
- the effect of competing technological and market developments; and
- other cash needs that may arise as we continue to operate our business.

We have no committed external sources of funding. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail our planned activities, including research and development programs and commercialization activities.

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

Until such time, if ever, as we can generate substantial product revenues, we expect to seek additional funding through a combination of equity offerings, debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. Additional funding may not be available to us on acceptable terms or at all.

The terms of any financing may adversely affect the holdings or the rights of our security holders. 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 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 entity. Prior to the commercial launch of Ocaliva for PBC in the United States in June 2016, in Canada in May 2017 and certain European countries in 2017, our operations were limited to developing our technology and undertaking preclinical studies and clinical trials of our product candidates and engaging in pre-commercial activities for Ocaliva in PBC. We do not have approval for any of our other product candidates.

While we commercially launched Ocaliva for PBC in the United States, Europe and certain other jurisdictions, we will need to conduct further activities to develop and cultivate a sustainable market for our drug in this orphan disease. These efforts will continue to be expensive and time-consuming, and we cannot be certain that we will be able to successfully develop a market. For example, we will need to conduct significant sales and marketing activities in jurisdictions where Ocaliva receives marketing approval. In the event we are unable to effectively develop and maintain a market for Ocaliva in PBC, our ability to effectively commercialize Ocaliva would be limited, and we would not be able to generate product revenues successfully.

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 or year-to-year due to a variety of factors, many of which are beyond our control. Factors relating to our business that may contribute to these fluctuations include:

- any delays in regulatory review and approval of our product candidates in clinical development;
- delays in the commencement, enrollment and timing of clinical trials;
- difficulties in identifying and treating patients suffering from our target indications, including those due to PBC and PSC being rare diseases and NASH currently requiring an invasive liver biopsy for diagnosis;
- the success of our clinical trials through all phases of clinical development, such as the success of our Phase 3 REGENERATE trial of OCA in non-cirrhotic NASH patients with liver fibrosis and our Phase 3 REVERSE trial of OCA in NASH patients with liver cirrhosis;
- potential side effects of Ocaliva and our other product candidates that could delay or prevent approval or cause an approved drug to be taken off the market;
- the required timeframe for us to receive and analyze data from our clinical trials;
- our ability to identify and develop additional product candidates;
- market acceptance of Ocaliva and our product candidates, which may be affected by the reimbursement that our products receive from payors;
- our ability to establish and maintain an effective sales and marketing infrastructure directly or through collaborations with third parties;
- competition from existing products or new products that may emerge;
- the ability of patients or healthcare providers to obtain coverage or reimbursement for our products and the extent to which such coverage or reimbursement will be provided;
- our ability to adhere to clinical trial requirements directly or with third parties such as contract research organizations, or CROs;
- our dependency on third-party manufacturers to manufacture our products and key ingredients;
- our ability to establish or maintain collaborations, licensing or other arrangements;
- the costs to us, and our ability and our third-party collaborators' ability to obtain, maintain and protect our intellectual property rights;
- costs related to and outcomes of potential intellectual property, securities and other litigation;
- our ability to adequately support future growth;
- our ability to attract and retain key personnel to manage our business effectively;
- our ability to build and improve our company's infrastructure, systems and controls;
- potential product liability claims; and
- our ability to obtain and maintain adequate insurance coverage.

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

We cannot be certain if Ocaliva will receive full approval for PBC in jurisdictions where it has received accelerated or conditional approval, or that Ocaliva will be approved for PBC in other jurisdictions. Furthermore, OCA may fail to become approved for any other indication and we may not be able to successfully 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 of a product candidate and issues relating to its approval and marketing are subject to extensive regulation by the FDA in the United States, the EMA in Europe and 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 revenue related to product sales will depend on the successful marketing of Ocaliva for PBC and the development and regulatory approval of OCA for the treatment NASH and our other product candidates.

Ocaliva is our only drug that has been approved for sale. In the United States, Ocaliva has been approved for PBC under the accelerated approval pathway. Accelerated approval was granted for OCA in PBC based on a reduction in alkaline phosphatase; however, an improvement in survival or disease-related symptoms has not been established. Continued approval of Ocaliva for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. Our Phase 4 COBALT confirmatory outcomes trial may fail to show a clinical benefit for OCA in PBC or may not satisfy the requirements of the regulatory authorities for other reasons.

As part of the 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 monotherapy in patients with PBC. Finally, we have also 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 after the European Commission granted conditional approval for Ocaliva for the treatment of PBC. The 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.

In May 2017, we received a marketing authorization with conditions for Ocaliva in PBC in Canada. We also plan to apply for marketing approval of Ocaliva for PBC in certain other markets across the world.

We currently have no other products approved for sale and we cannot guarantee that we will ever have additional marketable products or that our products will be approved for use in additional indications. 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 never guaranteed. Even after the submission of an NDA to the FDA, the FDA must decide whether to accept or reject the submission for filing. In addition, in June 2016, eligible members of the electorate in the United Kingdom decided by referendum to leave the European Union, or Brexit. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially change the regulatory regime applicable to our operations, including with respect to Ocaliva or our other product candidates.

Approvals may also 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 regulatory requests for additional analyses, reports, data, preclinical studies and clinical trials, regulatory questions regarding 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 other products. Regulatory approval is also dependent on successfully passing regulatory inspection of our company, our clinical sites and key vendors and to ensure compliance with applicable good clinical, laboratory and manufacturing practices regulation. Critical findings could jeopardize or delay the approval of an NDA or MAA.

We will also be required to finalize the negotiations and discussions on our product labels for the respective jurisdictions in which we seek regulatory approval. Even if a product is approved, the FDA or the EMA, as the case may be, may limit the indications or uses for which the 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 conditions of approval. Also, regulatory approval for any of our product candidates may be withdrawn. Regulatory authorities in countries outside of the United States and Europe also have requirements for approval of drug candidates with which we must comply prior to marketing in those countries. Obtaining regulatory approval for marketing of a product candidate in one country does not ensure that we will be able to obtain regulatory approval in any other country.

In order to obtain regulatory approval for OCA in indications other than PBC, we will need to complete a number of clinical trials and other studies for the continued development of OCA in indications other than PBC. For example, we currently have ongoing studies, including our Phase 3 REGENERATE trial of OCA in non-cirrhotic NASH patients with liver fibrosis and our Phase 3 REVERSE trial of OCA in NASH patients with cirrhosis. We also intend to conduct additional trials in NASH. In each of these cases, our ability to obtain the approvals necessary to commercialize OCA for such indications will depend on our ability to conduct and complete these additional trials as well as assemble various other data to complete our regulatory filings for OCA in the relevant indication or patient population.

There can be no assurance that we will be able to receive marketing approval for OCA in PBC in jurisdictions where it is not yet approved or marketing approval for OCA in NASH or any other indication. We cannot predict whether our trials and studies as to NASH or any other indication or patient population will be successful or whether regulators will agree with our conclusions regarding the preclinical studies and clinical trials we have conducted to date or require us to conduct additional studies or trials. For example, while OCA received breakthrough therapy designation from the FDA in January 2015 for the treatment of NASH patients with liver fibrosis, we do not know if one pivotal clinical trial will be sufficient for marketing approval or if regulators will ultimately agree to a surrogate endpoint for accelerated approval of OCA for the treatment of NASH. While the interim analysis for the REGENERATE trial will be based on a histological endpoint as was the case in the Phase 2b clinical trial for the treatment of NASH, known as the FLINT trial, sponsored by NIDDK, a part of the National Institutes of Health, our Phase 3 REGENERATE trial has different trial designs. For example, the primary endpoint for the interim analysis for REGENERATE may be achieved based on one of: (i) the proportion of OCA-treated patients relative to placebo achieving at least one stage of liver fibrosis improvement with no worsening of NASH or (ii) the proportion of OCA-treated patients relative to placebo achieving NASH resolution with no worsening of liver fibrosis. Furthermore, we selected a definition for NASH resolution for the trial, which defines a responder as a patient achieving a histologic score of 0 for ballooning and 0 or 1 for inflammation. The REGENERATE trial will also remain blinded after the interim analysis and 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.

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. 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. The baseline characteristics between the patients in the Japanese Phase 2 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 conducted by NIDDK. For example, differences were observed among the patient population at baseline in relation to gender mix and metabolic factors like weight, diabetes status, dyslipidemia and hypertension. While our REGENERATE trial was designed based on the results of the FLINT trial and is anticipated to enroll a predominantly Western NASH patient population, the results of the FLINT trial may not be replicated

in our REGENERATE trial. There is no assurance that Sumitomo Dainippon will initiate any registrational trials in NASH and the results of any additional trial conducted by Sumitomo Dainippon may not be an improvement as compared to those from the Phase 2 trial on Japanese NASH patients.

If we are unable to successfully commercialize OCA or obtain approval from the FDA, the EMA or other regulatory agencies for other product candidates or additional indications in OCA, we will 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, NASH and PSC, and for some of which there is little clinical experience, and our development approach involves new endpoints and methodologies. As a result, there is increased risk that we will not be able to gain agreement with regulatory authorities regarding an acceptable development plan, 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 treatments. As a result, the design and conduct of clinical trials for these diseases and other indications we may pursue will be subject to increased risk.

The FDA generally requires two 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 can grant accelerated approval based on a surrogate endpoint reasonably likely to predict clinical benefit. Even if results from our planned pivotal clinical trials for a specific indication are highly significant and we believe reasonably likely to predict clinical benefit, the FDA may not accept the results of such trials and grant accelerated approval of our product candidate for such indication.

Even if we receive accelerated approval for any of our product candidates, we may be required to conduct a post-approval clinical outcomes trial to confirm the clinical benefit of the product candidate by demonstrating the correlation of biochemical therapeutic response in patients with a significant reduction in adverse clinical outcomes over time. For example, we have received accelerated approval for OCA in PBC and now must undertake clinical outcome studies with respect to OCA in PBC. If any confirmatory clinical outcomes trials are required, as is the case for OCA in PBC, we may be required to have the trial be substantially underway at the time we submit an NDA. It is possible that our NDA submission for regulatory approval will not be accepted by the FDA for review or, even if it is accepted for review, that there may be delays in the FDA's review process and that the FDA may determine that our NDA does not merit the approval of the product candidate, in which case the FDA may require that we conduct and/or complete additional clinical trials and preclinical studies before it will reconsider our application for approval.

Following discussions with regulatory authorities, we initiated our COBALT clinical outcomes confirmatory trial in PBC in December 2014 prior to the approval of Ocaliva. The COBALT trial 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. There can be no assurance that our COBALT trial or other trials conducted as part of our post-marketing obligations will confirm that the surrogate endpoints used for accelerated approval 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 for Ocaliva in PBC.

We have agreed to similar requirements with the EMA as part of the conditional approval of Ocaliva in PBC in Europe. Our marketing authorization in the European Union for Ocaliva for the treatment of PBC is not a full approval and is conditional on post-approval studies. Our 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, including the completion of one or more clinical outcome trials to confirm the clinical benefit of Ocaliva in 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 (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. We may be required to conduct other post-marketing studies based on our regulatory interactions with other regulatory agencies across the world.

Our ongoing Phase 3 REGENERATE trial of OCA in non-cirrhotic NASH patients with liver fibrosis, incorporates an interim primary surrogate endpoint that may serve as the basis for a supplemental NDA filing for accelerated approval in the United States and approval in Europe. Accelerated approval in the United States and conditional approval in the European Union for OCA in NASH are subject to similar risks as discussed above in relation to OCA for PBC. The primary endpoint in the Phase 2b FLINT trial of OCA in NASH patients was based on liver biopsy and was defined as an improvement of two or more points in the NAS, with no worsening of liver fibrosis. In contrast, upon the finalization of a protocol amendment underway, the primary endpoint for the interim analysis for REGENERATE may be achieved based on one of: (i) the proportion of OCA-treated patients relative to placebo achieving at least one stage of liver fibrosis improvement with no worsening of NASH or (ii) the proportion of OCA-treated patients relative to placebo achieving NASH resolution with no worsening of liver fibrosis. Furthermore, we selected a definition for NASH resolution for the trial, which defines a responder as a patient achieving a histologic score of 0 for ballooning and 0 or 1 for inflammation. Currently, other biopharmaceutical companies are enrolling or have initiated trials in certain subpopulations of NASH patients based on different endpoints from those in the FLINT and REGENERATE trials. Although the FDA acknowledged at recent workshops the possibility of granting accelerated approval for NASH therapies using surrogate endpoints, with potential examples including histological improvement, using the NAS or another scoring system, histological resolution of NASH, or improvements in fibrosis in pre-cirrhotic patients with NASH, the FDA did not provide any formal regulatory guidance on approvable endpoints and may not accept a surrogate endpoint for OCA for the treatment of NASH.

It is possible that if we seek marketing approval of OCA for non-cirrhotic NASH patients with liver fibrosis based on the interim results of our REGENERATE trial, our NDA submission may not be accepted by the FDA for review or, even if accepted for review, there may be delays in the FDA's review process and the FDA may determine that our NDA does not merit the approval of OCA for the treatment of non-cirrhotic NASH patients. The FDA may also require that we continue our REGENERATE trial until its full completion to assess 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 designing an acceptable registration strategy around REGENERATE or any other trials in different subpopulations of NASH patients. In addition, since the design of the REGENERATE trial deviates from that of the FLINT trial, there is an increased risk that the results of the REGENERATE trial would differ from the FLINT results.

If we continue the development of OCA in PSC, we intend to seek marketing approval based on a surrogate endpoint. The FDA and EMA have not validated any surrogate endpoint as a basis for seeking approval in PSC and any surrogate endpoint we select may ultimately not be accepted by the regulatory agencies.

The EMA and regulatory authorities in other countries in which we may seek approval for, and market, OCA or our other product candidates may require additional preclinical studies and/or clinical trials prior to granting approval. It may be expensive and time consuming to conduct and complete additional preclinical studies and clinical trials that the FDA, EMA and other regulatory authorities may require us to perform. As such, any requirement by the FDA, EMA or other regulatory authorities 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 regulatory approval of OCA for the treatment of any of our targeted indications, the labeling for our product candidates in the United States, Europe or other countries in which we have received or seek approval may include limitations that could impact the commercial success of our product candidates.

Delays in the commencement, enrollment and completion of clinical trials could result in increased costs to us and delay or limit our ability to obtain regulatory approval for OCA and our other product candidates.

Delays in the commencement, enrollment and completion of clinical trials could increase our product development costs or limit the regulatory approval of our product candidates. We currently have underway a number of trials including our Phase 4 COBALT clinical outcomes confirmatory trial of OCA in PBC, our Phase 3 REGENERATE and REVERSE trials of OCA in NASH and our Phase 2 CARE trial of OCA in biliary atresia. We continue to work towards expanding our overall NASH development program with additional trials and studies, and we plan on conducting additional development activities in other diseases. The results from these trials may not be available when we expect or we may be required to conduct additional clinical trials or preclinical studies not currently planned to receive approval for OCA as a treatment for the related indication. In addition, our clinical programs are subject to a number of variables and contingencies, such as the results of other trials, patient enrollments or regulatory interactions that may result in a change in timing. As such, we do not know whether any future trials or studies in OCA or our other product candidates will begin on time or will be completed on schedule, if at all.

The commencement, enrollment and completion of clinical trials can be delayed or suspended for a variety of reasons, including:

- inability to obtain sufficient funds required for a clinical trial or lack of adequate funding to continue the clinical trial due to unforeseen costs or other business decisions;
- inability to reach agreements on acceptable terms with prospective CROs and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical holds, other regulatory objections to commencing or continuing a clinical trial or the inability to obtain regulatory approval to commence a clinical trial in countries that require such approvals;
- discussions with the FDA or non-U.S. regulators regarding the scope or design of our clinical trials, which may occur at various times, including subsequent to the initiation of the clinical trial;
- 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;
- the delay in receiving results from or the failure to achieve the necessary results in other clinical trials;
- inability to obtain approval from IRBs, to conduct a clinical trial at their respective sites;
- severe or unexpected drug-related adverse effects experienced by patients or any determination that a clinical trial presents unacceptable health risks;
- a breach of the terms of any agreement with, or for any other reason by, current or future collaborators that have responsibility for the clinical development of any of our product candidates, including Sumitomo Dainippon, or investigators leading clinical trials on our product candidates;
- inability to timely manufacture sufficient quantities of the product candidate required for a clinical trial;
- difficulty identifying, recruiting and enrolling patients to participate in clinical trials for a variety of reasons, including meeting the enrollment criteria for our trial, the rarity of the disease or condition, the rarity of the characteristics of the population being studied, the risks of procedures that may be required as part of the trial, such as a liver biopsy, and competition from other clinical trial programs for the same indications as our product candidates; and
- inability to retain enrolled patients after a clinical trial is underway.

For example, our REGENERATE trial is a large and complex Phase 3 clinical trial in a disease without any approved therapies and involves serial liver biopsies. While we announced the completion of enrollment of the interim analysis cohort in May 2017, and continuously evaluate and implement a variety of options to complete enrollment as quickly as possible, there can be no assurance that we will be able to enroll and retain a sufficient number of patients or complete the interim analysis and trial 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 complications that may negatively affect our plans or our development programs.

Additionally, we have in the past occasionally experienced difficulties retaining patients after enrollment in our clinical trials. Difficulty retaining patients may have, or may in the future, delay or produce negative or inconclusive results from our clinical trials, and we or our collaborators may decide, or regulators may require us, to conduct additional clinical trials or preclinical studies. 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.

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, Sumitomo Dainippon or our potential future collaborators advance through clinical trials may not have favorable results in later clinical trials or receive regulatory approval.

Clinical failure can occur at any stage of our 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 a product candidate. 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 a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well-advanced. We may be unable to design and execute a clinical trial to support regulatory approval. Further, clinical trials of potential products 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.

In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes or differences in trial protocols, differences in composition of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout 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 will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our product candidates. If we are unable to bring any of our current or future product candidates to market, or to acquire any marketed, previously approved products, our ability to create long-term stockholder value will be limited.

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

In December 2014, we received comprehensive datasets from the FLINT trial, which met its primary endpoint with statistical significance. In October 2015, we announced that the Phase 2 dose ranging trial of OCA in the Sumitomo Dainippon Phase 2 trial did not meet its primary endpoint with statistical significance. 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. The Phase 2 trial in NASH conducted in Japan by our collaborator Sumitomo Dainippon involved different doses of OCA being administered to the trial subjects than those utilized in FLINT. Furthermore, the baseline characteristics between the patients in the Japanese Phase 2 trial conducted by Sumitomo Dainippon were distinct in a number of ways from those of the Western patients included in FLINT. While our REGENERATE trial was designed based on the results of the FLINT trial and is anticipated to enroll a predominantly Western NASH patient population, the results of the FLINT trial may not be replicated in our REGENERATE trial. In addition, since the design of the REGENERATE trial deviates from that of the FLINT trial, there is an increased risk that the results of the REGENERATE trial would differ from the FLINT results. Even though OCA has been granted breakthrough therapy designation by the FDA, we do not know if one pivotal clinical trial will be sufficient for marketing approval or if regulators will agree to a surrogate endpoint for accelerated approval of OCA for the treatment of NASH. As a result, it may take longer than anticipated to initiate and complete the Phase 3 REGENERATE trial or our Phase 3 program in NASH for other patient subpopulations.

Our product candidates may have undesirable side effects which may delay or prevent marketing approval, or, if approval is received, require our product candidates to be taken off the market, require them to include safety warnings or otherwise limit their sales.

OCA has been shown to be a potent agonist of the FXR. With the exception of the endogenous human bile acid CDCA, 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 could arise either during clinical development or, if approved, after the approved product has been marketed.

The most common side effects observed in clinical trials of OCA in PBC were pruritus, or itching, fatigue, headaches, nausea, constipation and diarrhea. In our POISE trial, pruritus, generally mild to moderate, was the most frequently reported adverse event associated with OCA treatment and was observed in 38% of patients on placebo, 70% of patients in the 10 mg OCA 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%) patients were in the 10 mg OCA group and one (1%) patient 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 the POISE trial. In our Phase 2 trials for OCA in PBC, a dose-response relationship was observed for 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.

Ocaliva is contraindicated for PBC patients with complete biliary obstruction in the United States and the European Union. For patients with moderate or severe hepatic impairment, who represent approximately 3% of PBC patients, the U.S. label for Ocaliva in PBC includes an adjustment in the dosing regimen and the EU label recommends an adjusted dosing regimen due to potential exposure levels in this population. For 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 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 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 their own 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 have taken actions to enhance education about appropriate use of Ocaliva. These initiatives include: 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 completing adjudication of all 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 reinforce the 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 are working with relevant regulatory authorities, including the European Medicines Agency, or EMA, to ensure that the Ocaliva label in such jurisdictions sufficiently reinforces the importance of appropriate dosing in patients with advanced cirrhosis. These events and 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.

Based on information in the manuscript for the FLINT trial published in November 2014, pruritus occurred more frequently in the OCA treatment group than in the placebo treatment group (23% vs. 6%, $p < 0.001$) and at a higher grade (predominately moderate pruritus), but resulted in only one patient discontinuation in the OCA treatment group. In the FLINT trial, OCA treatment was 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. As previously disclosed, these changes in cholesterol levels, along with achieving the pre-defined efficacy criteria, played a role in the decision of the FLINT data and safety monitoring board to terminate the treatment phase of FLINT, and the publication of the FLINT results has noted the need for further study of these changes. There were two patient deaths in the FLINT trial, and neither death was considered related to OCA treatment.

In the Phase 2 CONTROL 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 5 mg OCA group, 10% of patients in the 10 mg OCA group and 55% of patients in the 25 mg OCA group. All events were mild to moderate and two patients discontinued treatment in the 25 mg OCA group due to pruritus. Over 95% of the patients completing the double-blind phase of CONTROL enrolled in the long-term safety extension phase, or LTSE phase, of the trial.

During the LTSE phase of CONTROL, there has been 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 25 mg OCA 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, or MRCP, 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 in PSC, pruritus was the most common adverse event, occurring in 46% of patients on placebo, 60% of patients in the 1.5 mg to 3 mg OCA group and 67% of patients in the 5 mg to 10 mg OCA group, with the severity increasing with dose. One (4%) patient in the 1.5 mg to 3 mg OCA group and three (12%) patients in the 5 mg to 10 mg OCA group discontinued OCA due to pruritus compared to none in the placebo group.

Additional or unforeseen side effects from 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 in PBC, OCA will be 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 NASH, PSC, biliary atresia and other potential indications. Furthermore, our commercial efforts for Ocaliva in PBC may be materially and adversely affected.

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

In addition, our drug candidates are being developed as potential treatments for severe, life threatening diseases and, as a result, our trials will necessarily be conducted in a patient population that will be more prone than the general population to exhibit certain disease states or adverse events. For example, as we expand our overall NASH development program, we intend to conduct trials in advanced patient populations, such as in our ongoing REVERSE trial in NASH patients with cirrhosis. Ocaliva is used 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 trials or in patients using commercial product were due to our drugs or drug candidates or some other factor, resulting in our company and our development programs being negatively affected even if such events or symptoms are ultimately determined to be unlikely related to our drugs and drug candidates. We further cannot assure you that additional or more severe adverse side effects with respect to OCA will not develop in future clinical trials or commercial use, which could delay or preclude regulatory approval of OCA or limit its commercial use.

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

- regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies;
- we may be required to change instructions regarding the way the product is administered, conduct additional clinical trials or change the labeling of the product;
- we may be subject to limitations on how we may promote the product;
- sales of the product may decrease significantly;
- regulatory authorities may require us to take our approved product off the market;

- we may be subject to litigation or product liability claims; and
- our reputation may suffer.

Breakthrough therapy designation for OCA may not lead to faster development or regulatory processes nor does it increase the likelihood that OCA will receive marketing approval for NASH.

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 any such qualification or ultimate marketing approval by the FDA.

In January 2015, we received breakthrough therapy designation for OCA in 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 for OCA in fibrotic NASH patients or increase the likelihood that OCA will be granted marketing approval for fibrotic NASH patients. Likewise, any future breakthrough therapy designation for 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 FDA for any such potential indication of OCA compared to drugs considered for approval under conventional FDA procedures. In addition, the FDA may withdraw any breakthrough therapy designation at any time. We may seek a breakthrough therapy designation for other of our product candidates, but the FDA may not grant this status to any of our proposed product candidates.

We may not be able to obtain or maintain orphan drug exclusivity for our product candidates, if approved, which would 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.

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 EMA or the FDA from approving another marketing application for the same product for that time period. The applicable period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified.

Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition. In addition, it is possible that orphan marketing exclusivity attaching to the marketing authorization will be reduced to six years if, at the end of the fifth year following the receipt of marketing authorization, the EMA and the Committee for Orphan Medicinal Products determine that the product does not satisfy the requisite criteria including demonstration of significant clinical benefit (having regard to requirements set out in the applicable EU regulations and guidance) where it is shown based on the available evidence that the product is sufficiently profitable to justify not to maintain the marketing exclusivity.

The failure to maintain orphan status may subject us to mandatory price discounts in Europe. In addition, our ability to launch in Europe may be delayed and we may lose 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 and EMA can subsequently approve another product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Any inability to secure orphan drug designation or the exclusivity benefits of this designation would have an adverse impact on our ability to develop and commercialize our product candidates.

We rely entirely on third parties for the manufacturing of our product candidates for preclinical studies, clinical trials and commercial supply of OCA. Our business could be harmed if those third parties fail to provide us with sufficient quantities of drug product, or fail to do so at acceptable quality levels or prices.

We do not intend to manufacture the pharmaceutical products that we plan to sell. We currently have agreements with a contract manufacturer for the production of the active pharmaceutical ingredients and the formulation of sufficient quantities of drug product for commercial sales and for our clinical trials and preclinical studies that we plan to conduct prior to and after seeking regulatory approval. If our contract manufacturer should cease to provide services to us for any reason, we likely would experience delays in advancing our clinical trials while we identify and qualify one or more replacement suppliers and we may be unable to obtain replacement supplies on terms that are favorable to us.

We currently have a long-term supply agreement with PharmaZell GMBH for the manufacture of commercial supply for Ocaliva. While we have procured sufficient supplies for the commercial launch of Ocaliva in PBC, we may not be able to procure sufficient supplies of Ocaliva on a continued basis. We are also seeking to qualify one or more back-up suppliers for our active ingredients; however, we may not be able to enter into additional long-term commercial supply agreements for OCA with other third-party manufacturers. We do not have agreements for long-term supplies of any of our other product candidates. We currently obtain these supplies and services from our third-party contract manufacturers on a purchase order basis.

Additionally, 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 the 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. If our manufacturers cannot successfully manufacture material that conform to our specifications and current good manufacturing practice requirements of any governmental agency whose jurisdiction to which we are subject, our products or product candidates will not be approved or, if already approved, may be subject to recalls.

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

- the possibility that we are unable to enter into or renew a manufacturing agreement with a third party to manufacture OCA or our product candidates;
- the possible breach of the manufacturing agreements by the third parties because of factors beyond our control; and
- the possibility of termination or nonrenewal of the agreements by the third parties before we are able to arrange for a qualified replacement third-party manufacturer.

Any of these factors could cause the delay of approval or disruption of commercialization of our products or product candidates, cause us to incur higher costs, prevent us from commercializing our products and product candidates successfully or disrupt the supply of our products after commercial launch. Furthermore, if any of our product candidates are approved and 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 our products and could lose potential revenue. It may take several years to establish an alternative source of supply and to have any such new source approved by the government agencies that regulate our products.

Even though we have received conditional approval of OCA to treat PBC in combination with ursodiol, we and our contract manufacturers are still subject to strict, ongoing regulatory requirements.

Even though we have received conditional approval of OCA for patients with PBC in combination with ursodiol in adults with an inadequate response to ursodiol or as monotherapy in adults unable to tolerate ursodiol, we and our contract manufacturers are subject to ongoing regulatory requirements for labeling, packaging, storage, advertising, promotion, record-keeping and submission of safety and other post-market information. In addition, we and our contract manufacturers and contract manufacturers' facilities are required to comply with extensive FDA and EMA requirements and requirements of other similar agencies, including ensuring that quality control and manufacturing procedures conform to current cGMPs. As such, we and our contract manufacturers are subject to continual review and periodic inspections to assess compliance with cGMPs. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. We are also required to report certain adverse reactions and production problems, if any, to the FDA and EMA and other similar agencies 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 must be consistent with the information in the product's approved label. Accordingly, we may not promote Ocaliva for indications or uses for which it is approved.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, it may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If our product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue Form FDA 483 notices or Warning Letters by the FDA or similar notices by other regulatory agencies;
- mandate modifications to 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 can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- recall our products
- suspend any ongoing clinical studies;
- impose other administrative or judicial civil or criminal penalties;
- withdraw regulatory approval, add label warnings or narrow the approved indication in the product label;
- refuse to approve pending applications or supplements to approved applications filed by us, Sumitomo Dainippon or our potential future collaborators;
- impose restrictions on operations, 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 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 these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, local, city, state or federal 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 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 healthcare provider letter and the FDA also subsequently issued its own safety communication to reinforce recommended dosing in accordance with the Ocaliva label. Both communications reminded 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 reinforce the 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 are working with relevant regulatory authorities, including the European Medicines Agency, or EMA, to ensure that the Ocaliva label in such jurisdictions sufficiently reinforces the importance of appropriate dosing in patients with advanced cirrhosis. The revised label, and any future label changes that may be required by the FDA or other relevant regulatory authorities in connection with Ocaliva and any safety concerns associated with Ocaliva, perceived or real, may adversely affect sales of Ocaliva.

We are subject to uncertainty relating to pricing and reimbursement. Failure to obtain or maintain adequate coverage and reimbursement for Ocaliva or our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford expensive treatments. 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 Ocaliva or our product candidates, if approved, depend and will depend substantially, both domestically and abroad, 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. Reimbursement policies could reduce the demand for, or the price paid for, our products.

We cannot be certain that reimbursement will be available for Ocaliva or any other products and product candidates that we develop. If reimbursement is not available or is available on a limited basis, we may not be able to successfully commercialize Ocaliva or any other products or product candidates that we develop.

In addition, third-party payors attempt to contain health care 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 cover or provide adequate payment for our products. We might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of our products or any other future products to such payors' satisfaction. Such studies might require us to commit a significant amount of management's time and our financial and other resources. Our products might not ultimately be considered cost-effective. Adequate third-party reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. The market for a drug will depend 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 branded drug in their formularies or otherwise 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. In addition, 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.

We do not know if the price we have selected for Ocaliva will receive broad acceptance from third-party payors. The coverage determination process may be a time-consuming and costly process that requires us to

provide scientific and clinical support for the use of Ocaliva in PBC to each payor separately, with no assurance that coverage will be obtained. If we are unable to obtain adequate coverage of Ocaliva from third-party payors, the adoption of Ocaliva by physicians and patients as a treatment for PBC may be limited. This in turn could affect our ability to successfully commercialize Ocaliva and adversely impact our profitability, results of operations, financial condition and future success.

Legislative healthcare reform may adversely affect our business.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or 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, or collectively, ACA, became law in the United States. Among other things, the purpose of the ACA is to reduce the cost of health care and substantially change the way health care 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 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 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. There is still uncertainty whether the ACA will undergo additional revisions, and we cannot predict the impact of any future modifications, and it is uncertain how any such proposals, if approved, would affect these provisions. 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, including a 2017 California law, currently being challenged, that would require manufacturers to provide advanced notification of price increases to certain purchasers and report specified drug pricing information to the state We cannot predict the success of 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 the product cannot be commercially launched until reimbursement is approved. The timing to complete the negotiation process in each country is highly uncertain. While we have been able to achieve rapid reimbursement decisions in some countries, as in the case in the United Kingdom, we expect that it may still require a number of months before we receive a reimbursement decision in many other countries. 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 generally 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 the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. We expect to experience pricing pressures in connection with the sale of OCA and any other products that we develop, 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 other product candidates, if approved, may not achieve broad market acceptance among physicians, patients and healthcare payors, and as a result our revenues generated from their sales may be limited.

The commercial success of Ocaliva or our other products or product candidates that we develop, if approved, will depend upon their acceptance among the medical community, including physicians, healthcare payors and patients. In order for Ocaliva to be commercially successful in PBC, we will need to demonstrate its utility as a treatment for patients who have an inadequate response to or who are unable to tolerate ursodiol, referred to as second line treatment, and show that it is more effective than any other alternatives that may be developed as a second line treatment for PBC, particularly given the much higher price that we charge for Ocaliva compared to the price of generically available ursodiol. 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. In NASH and PSC, since there are currently no approved therapies, we do not know the degree to which OCA will be accepted as a therapy, even if approved.

The degree of market acceptance of our product candidates will depend on a number of factors, including:

- limitations or warnings contained in our product candidates' FDA or EMA-approved labeling;
- changes in the standard of care or availability of alternative therapies at similar or lower costs for the targeted indications for any of our product candidates, such as ursodiol for the treatment of PBC;
- limitations in the approved clinical indications for our product candidates;
- demonstrated clinical safety and efficacy compared to other products;
- lack of significant adverse side effects;
- sales, marketing and distribution support;
- availability of reimbursement from managed care plans and other third-party payors;
- timing of market introduction and perceived effectiveness 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 product candidates are approved for inclusion on formularies of hospitals and managed care organizations;
- whether our product candidates are designated under physician treatment guidelines for the treatment of the indications for which we have received regulatory approval;
- adverse publicity about our product candidates or favorable publicity about competitive products;
- convenience and ease of administration of our product candidates; and
- potential product liability claims.

In addition, the potential market opportunity for our products and product candidates is difficult to precisely estimate. While ursodiol is the established standard of care for PBC, a majority of patients while on therapy remain at ALP levels above the ULN. According to our analysis of industry data in PBC, approximately 65% of patients treated with ursodiol experience elevated ALP levels, with approximately 35% of patients experiencing ALP levels greater than 1.67 times ULN. In addition, a small minority of PBC patients (estimated at approximately 3% of patients) are intolerant to ursodiol therapy. Our estimates of the potential market opportunity for Ocaliva for the treatment of PBC include a number of key assumptions related to prevalence rates, patients' access to healthcare, diagnosis rates and patients' response to or tolerance

of OCA, 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 in PBC could be smaller than our estimates of our potential market opportunity. If the actual market opportunity for Ocaliva or our product candidates is smaller than we expect, our product revenue may be limited.

If our product candidates are approved, but do not achieve an adequate level of acceptance by physicians, patients, the medical community and healthcare payors, sufficient revenue may not be generated from these products and we may not become or remain profitable. In addition, efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may never be successful.

We have limited sales, marketing or distribution experience and we will have 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. The commercial launch of Ocaliva for PBC represents our first product launch. We also plan to commercialize Ocaliva for PBC in certain other countries outside of the United States and Europe ourselves with a targeted sales force if we receive marketing approval. We may utilize the services of third-party collaborators in certain other jurisdictions. We have not yet decided on our commercialization strategy for OCA in other indications and for our other product candidates. 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 and time consuming and could delay any product launch. If the commercial launch of a product candidate 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 product candidates 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 direct sales and marketing efforts may not be successful.

We have a collaboration with Sumitomo Dainippon for the development and commercialization of OCA in China. We may have limited or no control over the sales, marketing and distribution activities of these third parties. Our future revenues may depend heavily on the success of the efforts of these third parties.

We will incur significant liability if it is determined that we are promoting any "off-label" use of Ocaliva.

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 for off-label uses. Accordingly, we may not promote Ocaliva in the United States for use in any indications other than for the treatment of patients with PBC in combination with ursodiol in adults with an inadequate response to ursodiol or as monotherapy in adults unable to tolerate ursodiol. The FDA and other regulatory and enforcement authorities actively enforce laws and regulations prohibiting promotion of off-label uses and 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 been the target of inquiries and investigations by various governmental authorities in the United States and abroad.

Notwithstanding the regulatory restrictions on off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional scientific exchange concerning their products. We intend to continue engaging in medical education activities and communicate with healthcare providers in compliance with all applicable laws, regulatory guidance and industry best practices.

While we have implemented a corporate compliance program based on what we believe are the current best practices, we cannot provide any assurance that governmental authorities will find that our business practices comply with current or future administrative or judicial interpretations of potentially applicable laws and regulations. If we fail to comply with any of these laws and regulations, we could be subject to a range of regulatory actions, including suspension or termination of clinical trials, the failure to approve a product candidate, restrictions on our products or manufacturing processes, withdrawal of Ocaliva or other products from the market, significant fines, disqualification or debarment from participation in federally-funded healthcare programs or other sanctions or litigation, any of which events may have a significant adverse impact on our business.

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

In addition to FDA restrictions on 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 such as 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 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.

The federal Health Insurance Portability and Accountability Act of 1996 or 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, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, 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, or PACA, require certain manufacturers of drugs, for which payment is available under certain federal health care 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 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 state laws differ from each other in significant ways, thus complicating compliance efforts.

Over the past few years, a number of pharmaceutical and other healthcare companies have been prosecuted under these laws for a variety of promotional and marketing activities, such as: 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 off-label promotion; and submitting inflated best price information to the Medicaid Rebate Program to reduce liability for Medicaid rebates.

We depend on collaborations with third parties, such as Sumitomo Dainippon, to develop and commercialize selected product candidates and have limited control over how those third parties conduct development and commercialization activities for such product candidates.

We selectively enter into collaboration agreements with third parties. We currently rely, and will continue to rely, on our collaborators for financial resources and for development, regulatory and commercialization expertise for selected product candidates, and we have limited control over the amount and timing of resources that our collaborators may devote to our product candidates.

Our collaborators may fail to develop or effectively commercial products using our product candidates or technologies for a variety of reasons, including that they:

- do not have sufficient resources or decide not to devote the necessary resources due to internal constraints such as limited cash or human resources or a change in strategic focus;
- decide to pursue a competitive product developed outside the collaboration; or
- cannot obtain the necessary regulatory approvals.

If any of our current strategic collaborators fails to perform its obligations or terminates its agreement with us, the development and commercialization of the products or product candidates under such agreement could be delayed or terminated and our business could be substantially harmed.

We currently have an exclusive license agreement with Sumitomo Dainippon regarding the development and commercialization of Ocaliva for PBC and OCA for NASH in China. This strategic collaboration may not be scientifically or commercially 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 under such agreement will depend on, among other things, the efforts, allocation of resources and successful development and commercialization of our product candidates by Sumitomo Dainippon under the agreement;
- Our agreement with Sumitomo Dainippon restricts it from developing or commercializing any FXR agonist to treat PBC or NASH during the term of the agreement other than pursuant to the

Sumitomo Dainippon agreement. Subject to these restrictions, 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 its strategic collaboration with us 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 rights licensed to them in their territories, and, although we may have the right to assume the maintenance and defense of our intellectual property rights if our strategic collaborator does not, our ability to do so may be compromised by our strategic collaborator's acts or omissions;
- Sumitomo Dainippon may utilize our intellectual property rights in such a way as to invite litigation that could jeopardize or invalidate our intellectual property rights or expose us to potential liability; and
- Sumitomo Dainippon may not comply with all applicable regulatory requirements, or fail to report safety data in accordance with all applicable regulatory requirements.

If Sumitomo Dainippon fails to develop or effectively commercialize OCA, we may not be able to replace it with another collaborator. For example, there is no assurance that Sumitomo Dainippon will initiate any registrational trials in NASH and the results of any additional trial conducted by Sumitomo Dainippon may not be an improvement as compared to those from the Phase 2 trial on Japanese NASH patients. We may also be unable to obtain, on terms acceptable to us, a license from such strategic collaborator to any of its intellectual property that may be necessary or useful for us to continue to develop and commercialize a product candidate. Any of these events could have a material adverse effect on our business, results of operations and our ability to achieve future profitability, and could cause our stock price to decline.

We may be adversely affected by the amendment of our exclusive license agreement with Sumitomo Dainippon.

On February 13, 2018, the Company entered into an amendment to its exclusive license agreement with Sumitomo Dainippon. Under the amendment, Sumitomo Dainippon agreed to return the rights to develop and commercialize OCA in Japan and Korea and we agreed to forego any further milestone or royalty payments for the development and commercialization of OCA in such countries. In addition, Sumitomo Dainippon waived its rights to the Country Option and the parties adjusted certain milestone payment obligations with respect to the development and commercialization of OCA. The parties also agreed that if certain clinical development milestones in China are not met by December 31, 2020, Sumitomo Dainippon may choose either to pay the Company a milestone payment or terminate the Agreement.

We may experience a decrease in revenue as a result of the amendment to our exclusive license agreement with Sumitomo Dainippon, as a result of potential foregone payments associated with such exclusive license agreement. Furthermore, we may not be successful in reaching an agreement with an alternative collaborator in the markets for which Sumitomo Dainippon had agreed to return its rights to develop and commercialize OCA, including Japan and Korea. In lieu of reaching an agreement with a suitable collaborator, we may independently develop and commercialize OCA in such markets ourselves and there is no guarantee that we would be successful in that endeavor.

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.

Because developing pharmaceutical products, conducting clinical trials, obtaining regulatory approval, expanding manufacturing capabilities and marketing approved products are expensive, we have entered into,

and may seek to enter into, collaborations with companies that have more experience and resources than we have. For example, we have entered into a collaboration with Sumitomo Dainippon for OCA with respect to China. We may establish additional collaborations for development and commercialization of OCA in territories outside of those licensed by Sumitomo Dainippon and for other product candidates and research programs, including INT-777. Additionally, if any of our product candidates receives marketing approval, we may enter into sales and marketing arrangements with third parties with respect to our unlicensed territories. If we are unable to maintain our existing arrangements or enter into any new such arrangements on acceptable terms, if at all, we may be unable to effectively market and sell our products in our target markets. We expect to face competition in seeking appropriate collaborators. Moreover, collaboration 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, we can expect to relinquish some or all of the control over the future success of that product candidate to the third party. For example, Sumitomo Dainippon has the exclusive rights to OCA in China. Our collaboration partner may not devote sufficient resources to the commercialization of our product candidates 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, including our collaboration with Sumitomo Dainippon, may be unsuccessful in the development and commercialization of our product candidates. In some cases, we may be responsible for continuing preclinical and initial clinical development of a product candidate or research program under a collaboration arrangement, 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 for our product candidates, we would face increased costs, we may be forced to limit the number of our product candidates we can commercially develop or the territories in which we commercialize them and we might fail to commercialize products or programs for which a suitable collaborator cannot be found. If we fail to achieve successful collaborations, our operating results and financial condition will be materially and adversely affected.

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

To date, we have focused the majority of our development efforts on the development of OCA. Among our other product candidates, only INT-767 is currently in clinical development. One of our strategies is to pursue clinical development of OCA in NASH and other progressive non-viral liver diseases, to the extent that we have sufficient funding.

PBC is an orphan disease. Since Ocaliva is indicated for use in PBC in combination with ursodiol in adults with an inadequate response to ursodiol or as monotherapy in adults unable to tolerate ursodiol, the market size is expected to be 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 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 for a long 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 commercialize OCA successfully.

The completion of development and securing of approval and commercialization of OCA for additional indications 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 FDA or EMA approval to market OCA for the treatment of any of these 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 these 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 the conduct of preclinical studies and clinical trials, collection and analysis of data and manufacturing. Although we are currently commercializing Ocaliva using our internal commercial organization, in the United States we are supporting our sales and marketing efforts with a small contract sales team and we will likely use the services of third-party vendors in relation to 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 the 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. Consequently, if these providers do not adhere to applicable governing practices and standards, the development and commercialization of Ocaliva and our other 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 to management oversight. 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 requested within the requested time periods. We subsequently replaced this manufacturer with other third-party contract manufacturers for OCA. 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 specialize or have the expertise required to achieve our business objectives. Identifying, qualifying and managing performance of third-party service providers can be difficult, time consuming and cause delays in our development programs. Despite our recent growth, we currently have a small number of employees, which limits the internal resources we have 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 in the future, our business may be adversely affected. We may further be subject to the imposition of civil or criminal penalties if their conduct of clinical trials 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 which 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 greater financial and other resources, such as larger research and development staff and more experienced marketing and manufacturing organizations. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and manufacturing pharmaceutical products. These companies also have significantly greater research, sales and marketing

capabilities and collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product candidates that we develop obsolete. As a result of all of these factors, our competitors may succeed in obtaining patent protection and/or FDA or EMA 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 we expect to compete with include Allergan Plc, AstraZeneca plc, Acorda Therapeutics, Inc., 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, Galectin Therapeutics Inc., Galmed Medical Research Ltd., Genfit SA, Gilead Sciences, Inc., GlaxoSmithKline, Immuron Ltd., Islet Sciences, Inc., Madrigal Pharmaceuticals, Inc., Metacrine, Inc., MiNA Therapeutics, NGM Biopharmaceuticals, Novartis International AG, Novo Nordisk A/S, Shire plc, Viking Therapeutics, Inc. and Zydus Pharmaceuticals Inc. Bezafibrate, a fibrate that has not been approved for commercialization by the FDA 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 GFT505, a dual PPAR alpha/delta agonist, in NASH. Genfit is also studying GFT505 for the treatment of PBC. Gilead Sciences, Inc. is conducting multiple Phase 3 clinical trials in NASH patients of various disease severity with selonsertib, an inhibitor of the apoptosis signal-regulating kinase 1. 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 and PSC. Allergan Plc has an ongoing Phase 3 clinical trial of cenicriviroc, an immunomodulator that blocks C-C chemokine receptor type 2 and type 5, 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 institutes may become active in our target disease areas. The results from our POISE and FLINT 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 obsolete and noncompetitive.

Off-label uses of other potential treatments may limit the commercial potential of our 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, though many fibrates are specifically contraindicated for use in PBC due to potential concerns over acute and long-term safety in this patient population. In NASH, a number of treatments, including vitamin E (an antioxidant), insulin sensitizers (e.g., metformin, pioglitazone), antihyperlipidemic agents (e.g., gemfibrozil), pentoxifylline and ursodiol, 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, similar improvements to those observed with OCA in the FLINT trial 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 reliability of Ocaliva and our other product candidates;
- the speed at which we develop our product candidates;

- our ability to design and successfully execute appropriate clinical trials;
- our ability to maintain a good relationship with regulatory authorities;
- the timing and scope of regulatory approvals, if any;
- our ability to commercialize and market any of our product candidates that receive regulatory approval;
- the price of our products;
- adequate levels of reimbursement under private and governmental health insurance plans, including Medicare;
- our ability to protect intellectual property rights related to our products;
- our ability to manufacture and sell commercial quantities of any approved products to the market; and
- acceptance of our product candidates by physicians and other health care providers.

If our competitors market products that are more effective, safer or less expensive than our future products, if any, or that reach the market sooner than our future products, if any, 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 each technology. 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 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 a wholly-owned subsidiary in the United Kingdom which serves as our headquarters for our international operations. We have also formed a number of other wholly-owned subsidiaries in Europe and Canada in preparation for the anticipated commercial launch of Ocaliva in PBC in those jurisdictions. Although we are currently commercializing Ocaliva using our internal commercial organization, we will likely use the services of third-party vendors in relation to our future commercialization activities, including product sales, marketing and distribution. In addition, we have entered into collaborations with Sumitomo Dainippon for the development of OCA, and we may enter into agreements with other third parties for the development and commercialization of OCA or our other product candidates in international markets. Our international operations and business relationships subject us to additional risks that may materially adversely affect our ability to attain or sustain profitable operations. We anticipate increasing our presence in international markets, subjecting us to many risks that could adversely affect our business and revenues, including:

- the far-reaching anti-bribery and anti-corruption legislation in the United Kingdom, including the 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 or pricing approvals of products in a timely manner;
- uncertainty regarding the collectability of accounts receivable;
- difficulties in staffing and managing international operations;
- potentially reduced protection for 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, e.g., a pharmacy, faced with relatively high local prices, 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 several countries in Europe;
- compliance with tax, employment, immigration and labor laws for employees traveling abroad;
- taxes in other countries;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from 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.

For example, we do not know the extent of the impact that the Brexit will have on our business. As a result of the Brexit, it is possible that Scotland and Northern Ireland may each conduct a referendum to decide whether to leave the United Kingdom. Furthermore, other European countries may seek to conduct referenda with respect to continuing membership with the European Union. We do not know to what extent these changes will impact our business. Our ability to conduct our international business out of the United Kingdom may be materially and adversely affected.

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, or the FCPA, and the UK Bribery Act. Generally, these prohibit paying or offering anything of value corruptly to any foreign government official, for the purpose of obtaining or retaining a business advantage. In many countries, the health care professionals we regularly interact with may meet the FCPA's definition of a foreign government official. U.S. and foreign regulators have increased their enforcement of anti-bribery and anticorruption laws in recent years. Failure to comply with these laws could result in various adverse consequences, including:

- possible delay in approval or refusal to approve a product;
- recalls, seizures or withdrawal of an approved product from the market;
- 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 sell products outside of the U.S. could adversely impact our business and financial results.

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 by taxing jurisdiction, the outcome of

examinations by the U.S. Internal Revenue Service and regulators of other jurisdictions, the accuracy of our estimates for unrecognized tax benefits, the realization of deferred tax assets, or by changes to our ownership or capital structure.

On December 22, 2017, the United States enacted tax reform legislation through the Tax Cuts and Jobs Act, which significantly changes the existing U.S. tax laws, including a reduction in the corporate tax rate to 21% effective for tax years including or commencing January 1, 2018, a move from a worldwide tax system to a territorial system, limitations on the deductibility of interest expense and executive compensation, as well as other changes.

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.

We have been significantly expanding our operations and the size of our company and will need to continue our expansion to support our future development strategy for OCA in other indications, including NASH, PSC and biliary atresia. We may experience difficulties in managing our significant growth.

We expect to continue to grow as we pursue additional pharmaceutical treatments for other indications. For example, from December 31, 2014 to December 31, 2017, our employee base has grown from 136 to 507 employees. As we advance our programs for OCA in NASH and other potential indications and our other product candidates, seek regulatory approval in the United States and elsewhere, increase the number of ongoing product development programs and advance our product candidates through preclinical studies and clinical trials, we will need to increase our product development, scientific and administrative headcount to manage these programs. We will also need to grow our commercial capabilities, which will require us to hire additional personnel for the launch and ongoing marketing and sale of Ocaliva in PBC and any product candidate for which we obtain marketing approval. Such an evolution may impact our strategic focus and our deployment and allocation of resources. Our management, personnel and systems currently in place 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 the anticipated longer-term growth in the other functions at our company, we will need to increase our general and administrative capabilities. We are also expanding our operations geographically and formed a number of wholly-owned subsidiaries outside of the United States. In addition to our U.S. offices, we also have an office in London, United Kingdom which serves as our headquarters for our operations in Europe and international markets, and regional offices in a number of these countries. In the longer term, we may further expand our geographical footprint. Our management, personnel and systems currently in place 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 will require in the United States, Europe and in other jurisdictions;
- manage our clinical programs effectively, which we anticipate being conducted at numerous clinical sites across the world, 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 this growth and adapt to this evolution in our strategic focus and increased complexity of operations, our business may be 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 across our organization due to the intense competition for qualified personnel and consultants 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 Mark Pruzanski, our co-founder and president and chief executive officer, and our other key employees and consultants. If we lose one or more of our executive officers, or key employees or consultants, our ability to implement our business strategy successfully could be seriously harmed. Any of our executive officers or key employees or consultants may terminate their employment at any time. Replacing executive officers, key employees and consultants may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize products successfully. 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 these additional key personnel and consultants.

We have scientific and clinical advisors and consultants, such as our co-founder Professor Roberto Pellicciari, 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 typically they 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 an increasingly demanding regulatory environment, which requires us to comply with the Sarbanes-Oxley Act of 2002, and the related rules and regulations of the Securities and Exchange Commission, expanded disclosure requirements, accelerated reporting requirements and more complex accounting rules. Company responsibilities required 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.

Our compliance with Section 404 of the Sarbanes-Oxley Act has required and will continue to require that we incur substantial accounting expense 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 so as to be able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act each year. If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner each year, we could be subject to sanctions or investigations by the Securities and Exchange Commission, 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 common stock. Furthermore, if we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed and investors could lose confidence in our reported financial information.

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 and non-U.S. regulators, provide accurate information to the FDA and non-U.S. regulators, comply with health care 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 health care industry are subject to extensive laws and regulations in the United States and abroad intended to prevent

fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. 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, 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 investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

We face potential product liability exposure, and if successful claims are brought against us, we may incur substantial liability for our products and product candidates and may have to limit 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 in 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, health care providers or others using, administering or selling our products. If we cannot successfully defend ourselves against any such claims, we would incur substantial liabilities. Regardless of merit or eventual outcome, product liability claims may result in:

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

We have obtained limited product liability insurance coverage in the United States for the use of OCA in our U.S. clinical trials and commercial sales and in selected other jurisdictions where we are conducting clinical trials. Our product liability insurance coverage in the United States is currently limited to an aggregate of $20.0 million. We have clinical trial and commercial product liability insurance coverage outside of the United States in amounts that vary by country. As such, 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. We intend to expand our insurance coverage for products to include the sale of commercial products if we obtain marketing approval for our product candidates in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. 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 will leave us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, employment practices liability, property, auto, workers'

compensation, products liability and directors' and officers' insurance. We do not know, however, if we will be able to maintain insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our financial position and results of operations. Furthermore, the increased volatility of our stock price may result in us being required to pay substantially higher premiums for our directors' and officers' insurance than those to which we are currently subject, and may even lead a large number of underwriters to be unwilling to cover us.

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

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 business 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' percentage ownership;
- incur substantial debt that may place strains on our operations;
- spend substantial operational, financial and management resources to integrate new products, technologies or businesses;
- assume substantial actual or contingent liabilities;
- reprioritize our development programs and even cease development and commercialization of our product candidates; or
- merge with, or otherwise enter into a business combination with, another company in which our stockholders would receive cash and/or shares of the other company on terms that certain of our stockholders may not deem desirable.

Although we intend to evaluate and consider in-license transactions, acquisitions, reorganizations and business combinations in the future, we have no agreements or understandings with respect to any acquisition, reorganization or business combination at this time.

We may use our financial and human resources to pursue a particular research program or product candidate and fail to capitalize on programs or product candidates that may be more profitable or for which there is a greater likelihood of success.

Because we have limited resources, we may forego or delay pursuit of opportunities with certain programs or product candidates or for indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for product candidates may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate where it would have been more advantageous to enter into a partnering arrangement.

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

Despite the implementation of security measures and policies, our internal information technology systems, as well as those of our CROs and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. 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. 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.

Although to date we have not experienced any material losses relating to cyber-attacks or other information security breaches, there can be no assurance that we will not suffer such losses in the future. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs, damage to our reputation and/or monetary damages. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

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, the 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 data. We adopted the EU-U.S. Privacy Shield and certified to its requirements in October 2016 and recertified in October 2017. In May 2018, the General Data Protection Regulation, or GDPR, will supersede current EU data protection legislation, impose more stringent EU data protection requirements, and provide for greater penalties for noncompliance. While we are actively employing the EU-U.S. Privacy Shield as a means to legitimize the transfer of personal information from the EU and Switzerland to the United States, and are engaging in activities to comply with the GDPR requirements, we may be unsuccessful in these efforts.

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 and product candidates, others could compete against us more directly, which would harm our business, possibly materially.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection of our current and future products and product candidates and the methods used to manufacture them, as well as successfully defending these patents against third-party challenges. Our ability to stop third parties from making, using, selling, offering to sell or importing our products and product candidates is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

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

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 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 or invalidity proceedings before U.S. or non-U.S. patent offices. Our patents may also be challenged under other proceedings, such as inter partes review and post-grant review proceedings introduced by provisions of the America Invents Act.

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 develop a platform similar to, or better than, ours in a way that is not covered by the claims of our patents;
- others may be able to make compounds that are similar to our products and product candidates but that are not covered by the claims of our patents;
- we might not have been the first to make the inventions covered by our pending patent applications;
- we might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- any patents that we obtain may not provide us with any competitive advantages;
- we may not develop additional proprietary technologies that are patentable; or
- the patents of others may have an adverse effect on our business.

As of December 31, 2017, we were the owner of record of over 110 issued or granted U.S. and non-U.S. patents relating to OCA with claims directed to pharmaceutical compounds, pharmaceutical compositions, methods of making these compounds, and methods of using these compounds in various indications. We were also the owner at that date of record of over 130 pending U.S. and non-U.S. patent applications relating to OCA in these areas.

In addition, as of December 31, 2017, we were the owner of record of approximately 230 issued or granted U.S. and non-U.S. patents relating to our product candidates other than OCA, with claims directed to pharmaceutical compounds, pharmaceutical compositions, methods of making these compounds and methods of using these compounds in various indications. We were also the owner of record of over 90 pending U.S. and non-U.S. patent applications relating to such other product candidates in these areas.

Patents covering the composition of matter of OCA expire in 2022 at the soonest and 2033 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, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, would expire from 2022 to 2033. We expect the issued INT-767 composition of matter patent in the United States, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire in 2029. We expect the other patents in the INT-767 portfolio, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire from 2027 to 2029. We expect the issued INT-777 composition of matter patent in the United States, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire in 2030. We expect the other patents in the INT-777 portfolio, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire from 2028 to 2030.

We have received assignments of rights to the INT-767 patent portfolio from all inventors, with the exception of one inventor. That inventor is contractually obligated to provide an assignment to us. Thus, we believe that we are the owner of the INT-767 patent portfolio by virtue of this contractual obligation and the patent assignments we have received. By virtue of the patent assignments we have received and other contractual obligations owed to us, we believe we are the owner of the INT-777 patent portfolio. Without patent protection on 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, or 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. 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.

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 and product candidates, U.S. patents may be eligible for limited extension of patent term under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as 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 the 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 and 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 OCA in PBC in May 2016, we have applied for an extension to the patent term for this patent in the United States through 2027. In addition, in connection with marketing authorization approval of OCA in PBC in the E.U, we have applied for supplementary patent certification to extend the patent term for this patent in the European Union through 2027. We expect to take similar actions in other jurisdictions and countries where similar regulations exist. In the event that we are unable to obtain any patent term extensions, the issued composition of matter patents for OCA are expected to expire in 2022 at the soonest and 2033 at the latest, assuming they withstand any challenge. We expect that the other patents for the OCA portfolio, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, would expire from 2022 to 2033.

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 managerial 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 managerial and scientific personnel even if we were successful in stopping the infringement of such patents. In addition, there is a risk that the court or adjudicating body will decide that such patents are not valid or not infringed, and that we do not have the right to stop the other party from using the inventions. There is also the risk that, even if the validity of such patents is upheld, the court or adjudicating body will refuse to stop the other party on the ground that such other party's activities do not infringe our rights to such patents. In addition, the U.S. Supreme Court has modified some tests used by the U.S. Patent and Trademark Office, or 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 product 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 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 collaborators 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 managerial and scientific personnel. There is a risk that a court would decide that we or our commercialization collaborators are infringing the third party's patents and would order us or our collaborators to stop the activities covered by the patents. In that event, we or our commercialization collaborators may not have a viable way around the patent and may need to halt commercialization of the relevant product. In addition, there is a risk that a court will order us or our collaborators to pay the other party damages for having violated the other party's patents. In the future, we may agree to indemnify our commercial collaborators against certain intellectual property infringement claims brought by third parties. The pharmaceutical and biotechnology industries have produced a proliferation of patents, and it is not always clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform.

If we are sued for patent infringement, we would need to demonstrate that our products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid, and we may not be able to do 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 these proceedings, we may incur substantial costs and divert management's time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, which may not be available, defend an infringement action or challenge the validity of the patents in court. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we fail to obtain a license, develop or obtain non-infringing technology or 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 the 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 or derivation proceeding declared by the USPTO to determine priority of invention in the United States. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful if, unbeknownst to us, the other party had independently arrived at the same or similar invention prior to our own invention, resulting in a loss of our U.S. patent position with respect to such inventions. Other countries have similar laws that permit secrecy of patent applications, and 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 resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations.

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

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ a third-party service provider and rely on this service provider to pay these fees due to the USPTO and non-U.S. patent agencies. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

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 and products 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. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

We rely on trade secrets to protect our proprietary technologies, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors 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. In addition, others may independently discover our trade secrets and proprietary information. For example, in September 2016, the Department of Health and Human Services adopted new regulations mandating sponsors to publicly post certain data from clinical trials of products subject to FDA regulation. Although the implementation of the regulations may be delayed, this and other transparency initiatives may result in making publicly available information we may consider to be trade secrets or proprietary information. Moreover, the EMA has already adopted a policy of general transparency both in relation to requests under EU freedom of information legislation for access to pre-clinical and clinical research data once marketing authorizations are granted and through proactive disclosure of clinical data on its website. This policy coupled with imminent requirements for public disclosure of clinical research data under a new EU Clinical Trial Regulation, means that public disclosure will ordinarily be made of substantial research data that previously would have been considered commercially confidential. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

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

We have applied for and obtained a number of trademarks and service marks to further protect the proprietary position of our products. As of December 31, 2017, we have over 630 trademark and service mark registrations and over 240 pending trademark and service mark applications in the United States and abroad.

Our trademark applications may not be allowed for registration or 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 to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many other jurisdictions, third parties are given 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 law, and continues 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 lead to customer confusion, which could adversely affect our sales or profitability.

We have received approval from both the FDA and EMA for Ocaliva®, the proprietary name for OCA, as well as the associated logo. The Ocaliva trademarks have registered in jurisdictions, including the United States, member states of the Community Trademark, Australia, Great Britain, New Zealand, Norway, Switzerland, Taiwan and certain other countries.

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 3.25% convertible senior notes due 2023 we issued in July 2016, or convertible notes or any 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 which 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 will not be restricted under the terms of the indenture governing the convertible notes from incurring additional debt, securing existing or future debt, recapitalizing our debt or taking a number of other actions that are not limited by the terms of the indenture governing the convertible notes that could have the effect of diminishing our ability to service our debt when due.

The conditional conversion feature of the convertible notes, if triggered, may adversely affect our financial condition and operating results.

In the event the conditional conversion feature of the convertible notes is triggered, holders will be entitled to convert their convertible notes at any time during specified periods at their option. If one or more holders elect to convert their convertible notes, unless we elect to satisfy our conversion obligation by delivering solely shares of our common stock (other than paying cash in lieu of delivering any fractional share), we would be required to settle a portion or all of our conversion obligation through the payment of cash, which could adversely affect our liquidity. In addition, even if holders do not elect to convert their

convertible notes, we could be required under applicable accounting rules to reclassify all or a portion of the outstanding principal of the convertible notes as a current rather than long-term liability, which would result in a material reduction of our net working capital.

The accounting method for convertible debt securities that may be settled in cash, such as the convertible notes, is the subject of recent changes that could have a material effect on our reported financial results.

Under Accounting Standards Codification 470-20, Debt with Conversion and Other Options, which we refer to as ASC 470-20, an entity must separately account for the liability and equity components of the 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 would be treated as original issue discount for purposes of accounting for the debt component of the convertible notes. As a result, we will be 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. We will report lower net income in our financial results because ASC 470-20 will require interest to include both the current period's amortization of the debt discount and the instrument's coupon interest, which could adversely affect our reported or future financial results, the trading price of our common stock and the trading 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.

Provisions in the indenture governing the convertible notes may deter or prevent a business combination that may be favorable to you.

If a fundamental change occurs prior to the maturity date of the convertible notes, holders of the convertible notes will have the right, at their option, to require us to repurchase all or a portion of their convertible notes. In addition, if a make-whole fundamental change occurs prior to the maturity date of the convertible notes, we will in some cases be required to increase the conversion rate for a holder that elects to convert its convertible notes in connection with such make-whole fundamental change. Furthermore, the indenture governing the convertible notes prohibits us from engaging in certain mergers or acquisitions unless, among other things, the surviving entity assumes our obligations under the convertible notes and the indenture. These and other provisions in the indenture could deter or prevent a third party from acquiring us even when the acquisition may be favorable to you.

Risks Related to Ownership 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 our stockholders' 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. As of December 31, 2017, approximately 30% of our outstanding shares of common stock was held by our officers, directors, beneficial owners of 5% or more of our securities (other

than FMR LLC, Capital World Investors, Ameriprise Financial, Inc., JPMorgan Chase & Co., The Vanguard Group and their respective affiliates) and their respective affiliates, which adversely affects the liquidity of the trading market for our common stock, in as much as federal securities laws restrict sales of our shares by these stockholders. If our affiliates continue to hold their shares of common stock, there will be limited trading volume in our common stock, which may make it more difficult for investors to sell their shares or increase the volatility of our stock price.

We were previously subject to securities class action litigation and may be subject to similar or other litigation in the future, which may divert management's attention.

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.

A lawsuit and follow-on lawsuit have been filed alleging, among other things, that we and certain of our officers violated federal securities laws by making allegedly material false and/or misleading statements regarding our business, operational and compliance policies. The plaintiff seeks unspecified monetary damages on behalf of the putative class and an award of costs and expenses, including attorney's fees. In addition, a lawsuit has been filed alleging, among other things, that our directors breached their fiduciary duties in connection with the Company's non-executive director compensation practices. The lawsuit seeks money damages and an order directing the Company to take all necessary actions to reform and improve its corporate governance and internal procedures relating to non-employee director compensation, as well as equitable and injunctive relief, restitution and costs and fees. While we believe we have meritorious defenses and intent to rigorously defend ourselves, we cannot predict the outcome of this lawsuit.

There may be additional suits or proceedings brought in the future. Monitoring and defending against legal actions, whether or not meritorious, is 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 these matters. In addition, we may incur substantial legal fees and costs in connection with litigation. 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 and the Convertible Notes to incur substantial losses.

The trading 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 initial public offering which occurred 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, these factors include:

- failure to successfully commercialize Ocaliva for PBC in jurisdictions where we have received marketing authorization or our inability to receive marketing approval for Ocaliva in other jurisdictions;
- adverse results or delays in our clinical trials;
- inability to obtain additional funding;
- any delay in filing an IND, NDA, MAA or comparable submission for any of our products and product candidates and any adverse development or perceived adverse development with respect to the regulatory review of such submission;

- failure to successfully develop and commercialize OCA for indications other than PBC and any of our other product candidates;
- inability to obtain adequate product supply for OCA and our future product candidates or the inability to do so at acceptable prices;
- results of clinical trials of our competitors' products;
- regulatory actions with respect to our products or our competitors' products;
- changes in laws or regulations applicable to our products or future products;
- failure to meet or exceed financial projections we may provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;
- 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;
- significant lawsuits, including patent, stockholder or product liability litigation, involving us;
- 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;
- market conditions for biopharmaceutical stocks in general; and
- general economic, industry and market conditions.

Furthermore, the 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 the target of 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, our stockholders could incur substantial losses.

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 S.p.A. and its affiliates, or, collectively, 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.

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

Genextra is our largest stockholder. As of December 31, 2017, Genextra owned 6,454,953 shares of our common stock. The shares of common stock owned by Genextra represented approximately 26% of our outstanding common stock as of December 31, 2017. 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 any other holder of common stock or directors of our business 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 prevailing market price for our common stock. Our board of directors, which consists of nine 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 share of our common stock into the market from time to time. If we in the future engage in a registered offering of our common stock, we could also determine, as we have done in the past, to register for sale a portion of Genextra's shares as part of that same offering to provide for the orderly sale of such shares. We cannot predict the effect, if any, that future sales by Genextra may have on the market price for 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.

In the future, we may issue additional shares of our common stock or other securities convertible into or exchangeable for our common stock in order to raise additional capital or in connection with strategic transactions, including potential in-licenses or acquisitions of products, technologies or businesses. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share you paid for our shares. If we issue securities in connection with

a strategic transaction, we cannot assure you that the value of the assets we receive will be commensurate with the value of the securities we may issue. Investors purchasing or otherwise acquiring shares or other securities from us in the future could have rights, preferences or privileges senior to those of existing stockholders and you may experience dilution. You may also incur additional dilution upon the exercise of any outstanding stock options or vesting of restricted stock units or awards.

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 our stock, the price of our stock and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about 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 would likely decline. If one or more of the analysts covering us fail to regularly publish reports on us, demand for our common stock could 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, might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock.

Provisions in our restated certificate of incorporation and restated bylaws, as well as provisions of Delaware law, contain provisions that may discourage, delay or prevent a merger, acquisition or other change in control that stockholders may 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, or 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.

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, provided, however, that such advance payment will only be made upon delivery to us of an undertaking, by or on behalf of the director or officer, to repay all amounts so advanced if it is ultimately determined that such director is not entitled to indemnification. If we do not pay a proper claim for indemnification in full within 60 days after we receive a written claim for such indemnification, except in the case of a claim for an advancement of expenses, in which case such period is 20 days, our restated certificate of incorporation and our restated bylaws authorize the claimant to bring an action against us and prescribe what constitutes a defense to such action.

Section 145 of the DGCL permits a corporation to indemnify any director or officer of the corporation against expenses (including attorney's fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with any action, suit or proceeding brought by reason of the fact that such person is or was a director or officer of the corporation, if such person acted in good faith and in a manner that he reasonably believed to be in, or not opposed to, the best interests of the corporation, and, with respect to any criminal action or proceeding, if he or she had no reason to believe his or her conduct was unlawful. In a derivative action (i.e., one brought by or on behalf of the corporation), indemnification may be provided only for expenses actually and reasonably incurred by any director or officer in connection with the defense or settlement of such an action or suit if such person acted in good faith and in a manner that he or she reasonably believed to be in, or not opposed to, the best interests of the corporation, except that no indemnification shall be provided if such person shall have been adjudged to be liable to the corporation, unless and only to the extent that the court in which the action or suit was brought shall determine that the defendant is fairly and reasonably entitled to indemnity for such expenses despite such adjudication of liability.

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. We have entered into indemnification agreements with each of our officers and directors.

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 have increased the coverage under our 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.

To date, we have not paid any cash dividends on our common stock, and we do not intend to pay any dividends in the foreseeable future. Instead, we intend to retain earnings to fund the development and growth of our business. For this reason, the success of an investment in our common stock, if any, will depend on the appreciation of our common stock, which may not occur. There is no guarantee that our common stock will appreciate, and therefore, a holder of our common stock may not realize a return on his or her investment.

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

As of December 31, 2017 and 2016, we had net operating loss carryforwards, or NOLs, for U.S. Federal income tax purposes of $628.0 million and $562.3 million, respectively, which expire between 2024 and 2037. We also have certain state and foreign NOLs in varying amounts depending on the different state and foreign tax laws.

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. Additionally, tax laws limit the time during which NOLs and certain other tax attributes may be utilized against future taxes. 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 is located in New York, New York, where we lease and occupy an aggregate of approximately 45,500 square feet of office space. The lease for our current corporate headquarters will expire in July 2021. In December 2017, we terminated the lease agreement relating to 55 Hudson Yards and have chosen to stay in our current 10 Hudson Yards location in order to reduce our long-term lease obligations. We incurred $9.8 million in expenses, which included a $7.8 million termination fee.

Our research and development operations are located in San Diego, California, where we lease and occupy approximately 47,000 square feet of space. The lease ends in September 2019; however, we have an option to further extend the lease for an additional five-year term at market rates prevailing at such time.

Our wholly owned subsidiary, Intercept Pharma Europe Ltd., or IPEL, also leases and occupies 8,500 square feet of office space in the King's Cross area of London, United Kingdom for our international headquarters. The lease expires in May 2024. We are the guarantor to IPEL's underlease for our international headquarters.

Item 3. Legal Proceedings

See Item 1. "Business — Legal Proceedings" of this Annual Report.

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

Our common stock began trading on the Nasdaq Global Market on October 11, 2012 under the symbol "ICPT". The following table sets forth, for the quarterly periods indicated, the high and low sales prices per share of our common stock as reported on the Nasdaq Global Select Market for each quarter in the years ended December 31, 2017 and 2016.

Year Ended December 31, 2017	High	Low
First quarter	$ 135.25	$ 101.99
Second quarter	133.73	104.33
Third quarter	135.59	54.98
Fourth quarter	75.80	57.25

Year Ended December 31, 2016	High	Low
First quarter	$ 152.60	$ 89.76
Second quarter	173.31	127.45
Third quarter	177.93	140.38
Fourth quarter	166.12	96.63

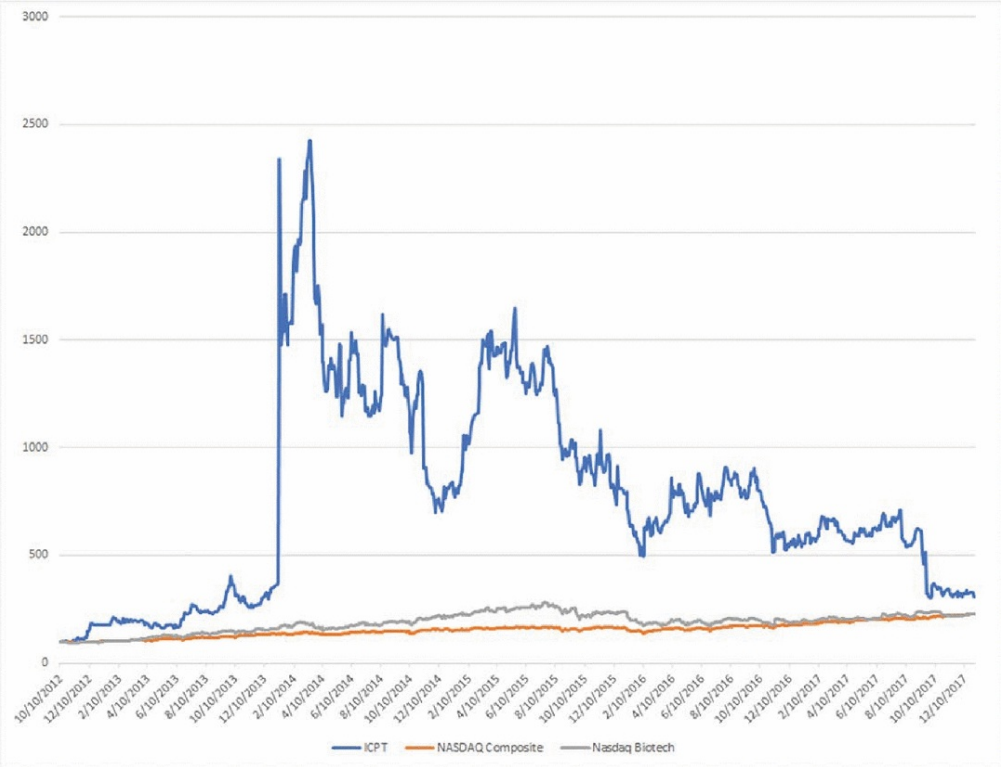
Stockholders

As of December 31, 2017, there were 454 stockholders of record, which excludes stockholders whose shares were held in nominee or street name by brokers.

Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return for our common stock from October 11, 2012 through December 31, 2017 to two indices: the Nasdaq Composite Index and the Nasdaq Biotechnology Index. The graph assumes an initial investment of $100 on October 10, 2012 in our common stock, the stocks comprising the Nasdaq Composite Index, and the stocks comprising the Nasdaq Biotechnology Index and it assumes the reinvestment of dividends, if any. Historical stockholder return is not necessarily indicative of the performance to be expected for any future periods.

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



* $100 invested on 10/10/2012 in stock or index. Fiscal Year ending December 31, 2017.

The performance graph shall not be deemed to be incorporated by reference by means of any general statement incorporating by reference this Annual Report into any filing under the Securities Act of 1933, as amended, or Securities Act, or Exchange Act, except to the extent that we specifically incorporate such information by reference, and shall not otherwise be deemed filed under such acts.

Dividend Policy

We have never paid or declared any cash dividends on our common stock, and we do not anticipate paying any cash dividends on our common stock in the foreseeable future. We intend to retain all available funds and any future earnings to fund the development and expansion of our business. Any future determination to pay dividends will be at the discretion of our board of directors and will depend upon a number of factors, including our results of operations, financial condition, future prospects, contractual restrictions, restrictions imposed by applicable law and other factors our board of directors deems relevant.

Securities Authorized for Issuance Under Equity Compensation Plans

The information required by Item 201(d) of Regulation S-K is incorporated by reference to Item 12. “Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters” of this Annual Report.

Recent Sales of Unregistered Securities

We did not sell any securities that were not registered under the Securities Act in the last three fiscal years.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report.

Item 6. Selected Financial Data

The selected financial data set forth below is derived from our audited consolidated financial statements. The following selected consolidated financial data should be read in conjunction with Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the consolidated financial statements and the notes thereto included elsewhere in this Annual Report. The selected financial data in this section are not intended to replace our consolidated financial statements and the related notes. Our historical results are not necessarily indicative of our future results.

	Years Ended December 31,				
	2017	2016	2015	2014	2013
	(in thousands, except per share data)				
Statement of Operations Data:					
Total revenues	$ 130,956	$ 24,951	$ 2,782	$ 1,742	$ 1,622
Operating expenses:					
Cost of Sales	1,371	—	—	—	—
Selling, general and administrative	273,698	273,596	119,242	34,601	13,132
Research and development	191,499	153,893	112,696	80,311	27,941
Total operating expenses	466,568	427,489	231,938	114,912	41,073
Loss from operations	(335,612)	(402,538)	(229,156)	(113,170)	(39,451)
Total other income (expense), net	(24,755)	(10,292)	2,727	(170,056)	(28,341)
Net loss	(360,367)	(412,830)	(226,429)	(283,226)	(67,792)
Dividend on preferred stock, not declared	—	—	—	—	—
Net loss attributable to common stockholders	$(360,367)	$(412,830)	$(226,429)	$(283,226)	$ (67,792)
Net loss per share, basic and diluted	$ (14.38)	$ (16.74)	$ (9.56)	$ (13.63)	$ (3.76)
Weighted average shares outstanding, basic and diluted	25,054	24,663	23,694	20,784	18,029

	December 31,				
	2017	2016	2015	2014	2013
	(in thousands)				
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 414,917	$ 689,385	$ 628,055	$ 239,724	$ 144,832
Total assets	484,347	739,253	655,758	254,149	150,319
Accounts payable, accrued expenses and other liabilities	94,777	65,551	45,591	13,459	7,260
Warrant liability	—	—	—	—	50,112
Long-term debt	355,677	341,356	—	—	—
Accumulated deficit	(1,469,543)	(1,108,460)	(695,630)	(469,202)	(185,976)
Total stockholders' equity	16,386	314,932	602,149	230,891	82,406

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors. We discuss factors that we believe could cause or contribute to these differences below and elsewhere in this Annual Report, including those set forth under Item 1.A "Risk Factors" and under "Forward-Looking Statements" in this Annual Report.

Overview

We are a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat non-viral, progressive liver diseases with high unmet medical need utilizing our proprietary bile acid chemistry. Our marketed product and clinical product candidates have the potential to treat orphan and more prevalent liver diseases for which, currently, there are limited therapeutic solutions.

OCA was approved in the United States in May 2016 as a treatment for use in patients with PBC, under the brand name Ocaliva. 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 the farnesoid X receptor, or FXR. We believe OCA has broad liver-protective properties and may effectively counter a variety of chronic insults to the liver that cause fibrosis, or scarring, which can eventually lead to cirrhosis, liver transplant and death.

We commenced sales and marketing of Ocaliva in the United States shortly after receiving such marketing approval, and Ocaliva is now available to patients primarily through a network of specialty pharmacy distributors. 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. We have submitted or are in the process of submitting dossiers to a number of reimbursement authorities in the European Union. In May 2017, Health Canada granted a conditional approval for Ocaliva in PBC and we commenced our commercial launch in July 2017. We also plan to file for marketing authorization for OCA in PBC in other target markets.

We are currently evaluating our future development strategy for OCA in other indications, including a variety of other non-viral progressive liver diseases such as nonalcoholic steatohepatitis, or NASH, primary sclerosing cholangitis, or PSC, and biliary atresia.

OCA achieved the primary endpoint in a Phase 2b clinical trial for the treatment of NASH, known as the FLINT trial, which was sponsored by the U.S. National Institute of Diabetes and Digestive and Kidney Diseases, or NIDDK, a part of the National Institutes of Health. The FLINT trial was completed in late July 2014. We have an ongoing Phase 3 clinical trial in non-cirrhotic NASH patients with liver fibrosis, known as the REGENERATE trial. REGENERATE includes a pre-planned histology-based interim analysis after 72 weeks of treatment. In May 2017, we completed enrollment of the interim analysis cohort for the REGENERATE trial. We anticipate top-line results from the interim analysis in the first half of 2019. We have also completed a Phase 2 clinical trial, known as the 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. We announced that this trial met its primary endpoint in July 2017. We 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, which we announced in February 2018.

In addition to PBC and NASH, we continue to invest in research of OCA for additional patient populations with other liver diseases. For example, in July 2017, we announced top-line results of our Phase 2 AESOP trial in PSC which evaluated the effects of 24 weeks of treatment with varying doses of OCA compared to placebo. This trial achieved its primary endpoint, which we believe establishes a proof-of-concept of OCA in a second cholestatic liver disease. We plan to discuss these results with regulatory authorities to formulate our future development plans for OCA in PSC.OCA has received orphan drug designation in the

United States and the European Union for the treatment of PBC and PSC and breakthrough therapy designation from the U.S. Food and Drug Administration, or FDA, for the treatment of NASH patients with liver fibrosis.

Our current patents for OCA are scheduled to expire at various times through 2033. We own or have rights to various trademarks, copyrights and trade names used in our business, including rights to OCA worldwide except for China, where we have exclusively licensed OCA to Sumitomo Dainippon.

Our net loss for the years ended December 31, 2017 and 2016 was approximately $360.4 million and $412.8 million, respectively. As of December 31, 2017, we had an accumulated deficit of approximately $1.5 billion. Substantially all of our net losses resulted from costs incurred in connection with our research and development programs and from selling, general and administrative costs associated with our operations.

We expect to continue to incur significant expenses and operating losses for at least the next several years as we:

- continue to commercialize Ocaliva for PBC in the United States, Europe and other jurisdictions where it has received marketing approval;
- seek regulatory approval for and prepare to commercially launch Ocaliva for PBC in other target markets;
- develop and seek regulatory approval for OCA in NASH and other indications; and
- add infrastructure and personnel in the United States and internationally to support our product development and commercialization efforts and operations as a public company.

We anticipate that we will need to raise additional capital to commercialize OCA on a worldwide basis and continue our research and development activities in relation to OCA and our other pipeline candidates. Until we are able to consistently generate profits from our operations, we expect to finance our operating activities through a combination of equity offerings, debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise additional capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our product candidates.

Recent Developments

Sumitomo Dainippon License Amendment

On February 13, 2018, the Company entered into an amendment to its exclusive license agreement with Sumitomo Dainippon. Under the amendment, Sumitomo Dainippon agreed to return the rights to develop and commercialize OCA in Japan and Korea and we agreed to forego any further milestone or royalty payments for the development and commercialization of OCA in such countries. In addition, Sumitomo Dainippon waived its option rights to develop OCA in any country outside of China and the parties adjusted certain milestone payment obligations with respect to the development and commercialization of OCA. The parties also agreed that if certain clinical development milestones in China are not met by December 31, 2020, Sumitomo Dainippon may choose either to pay the Company a milestone payment or terminate the Agreement.

55 Hudson Yards Lease

In December 2017, we terminated the lease agreement relating to 55 Hudson Yards and have chosen to stay in our current 10 Hudson Yards location in order to reduce our long-term lease obligations. We incurred $9.8 million in expenses, which included a $7.8 million termination fee.

Financial Overview

Revenue

We commenced our commercial launch of Ocaliva for use in 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. In May 2017, Health Canada granted a conditional approval for Ocaliva in PBC and we commenced our commercial launch in July 2017.

Revenue is recognized when the four basic criteria of revenue recognition are met: (1) persuasive evidence that an arrangement exists; (2) delivery has occurred or services have been rendered; (3) the fee is fixed or determinable; and (4) collectability is reasonably assured. When the revenue recognition criteria are not met, we defer the recognition of revenue by recording deferred revenue on the balance sheet until such time that all criteria are met.

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 had 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 to 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 had accumulated sufficient data to reasonably estimate product returns and, therefore, we now effectively 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 nine months ended September 30, 2017. We also established a new reserve of $0.7 million during third quarter of 2017 related to future returns from our customers under our various contracts.

We have written contracts with each of our customers and delivery occurs when the customer receives Ocaliva. We evaluate the creditworthiness of each of our customers to determine whether collection is reasonably assured. In order to conclude that the price is fixed and determinable, we must be able to (i) calculate our gross product revenues from the sales to our customers and (ii) reasonably estimate our net product revenues. We calculate gross product revenues based on the wholesale acquisition cost that we charge our customers for Ocaliva. We estimate net product revenues by deducting from our gross product revenues (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.

Licensing Revenue

We recognize revenue derived from our collaborative agreements for the development and commercialization of certain of our product candidates. In March 2011, we entered into an exclusive licensing agreement with Sumitomo Dainippon for the development of OCA in certain countries outside the United States. Under the terms of the agreement, we have received up-front payments totaling $16.0 million, including $1.0 million upon the exercise by Sumitomo Dainippon in May 2014 of its option to add Korea to its licensed territories. Following the amendment to the agreement in February 2018, Sumitomo Dainippon may be required to pay us up to an aggregate of approximately $4 million for the achievement of development milestones, $19 million for the achievement of regulatory approval milestones and tiered royalties up to the mid-twenties in percentage terms based on net sales of OCA products in China. As of December 31, 2017, we have achieved $6.0 million of the development and regulatory milestones.

For accounting purposes, the up-front payments are recorded as deferred revenue and amortized over time and milestone payments are recognized once earned. We recognized $1.8 million and $6.8 million, respectively, in license revenue resulting from milestone payments and the amortization of the up-front payments under the collaboration agreement for the years ended December 31, 2017 and 2016. We anticipate

that we will recognize revenue of approximately $1.8 million per year through 2020, for the amortization of the relevant up-front collaboration payments from Sumitomo Dainippon.

Selling, General and Administrative Expenses

Our selling, general and administrative expenses, excluding the one-time net expense of $45.0 million attributable to the settlement of a purported securities class action lawsuit in 2016, have increased and we expect to continue to incur significant expenses due to the commercialization of Ocaliva for PBC in the United States, Europe and certain other countries, the potential commercialization of OCA in PBC in other international markets and development activities for OCA in indications other than PBC and other product candidates. We further plan on expanding our operations both in the United States and abroad, which will increase our selling, general and administration expenses. We believe that these activities will result in costs related to the hiring of additional personnel, fees for outside consultants, lawyers and accountants, and the maintenance of facilities. We have also incurred and expect to continue to incur increased costs to comply with corporate governance, internal controls, compliance and similar requirements applicable to public companies with expanding operations and biopharmaceutical companies undertaking worldwide product launches.

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, manufacturing development efforts and activities related to regulatory filings for our product candidates. We recognize research and development expenses as they are incurred.

Our research and development expenses have increased and we expect to continue to incur significant expenses due to our preclinical studies and clinical trials and other research and development efforts. We anticipate that our research and development expenses will be substantial for the foreseeable future as we continue the development of OCA for the treatment of PBC, NASH and PSC and other indications and to further advance the development of our other product candidates, subject to the availability of additional funding.

Results of Operations

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, together with the changes in those items in dollars and as a percentage:

	Years Ended December 31,		Dollar	
	2017	2016	Change	% Change
	(in thousands)			
Revenue:				
Product revenue, net	$ 129,175	$ 18,169	$ 111,006	611%
Licensing revenue	1,781	6,782	(5,001)	-74%
Total revenue	130,956	24,951	106,005	425%
Operating expenses:				
Cost of Sales	1,371	—	1,371	N/M
Selling, general and administrative	273,698	273,596	102	0%
Research and development	191,499	153,893	37,606	24%
Total operating expenses	466,568	427,489	39,079	9%
Other income (expense):				
Interest expense	(29,271)	(14,196)	(15,075)	106%
Other income, net	4,516	3,904	612	16%
Total other income (expense)	(24,755)	(10,292)	(14,463)	141%
Net loss	$(360,367)	$(412,830)	$ 52,463	-13%

* N/M = not meaningful.

Revenues

Product revenue, net was $129.2 million and $18.2 for the years ended December 31, 2017 and 2016, respectively. We commenced our commercial launch in the United States for Ocaliva in PBC in June 2016. For the years ended December 31, 2017 and 2016, licensing revenue was $1.8 million and $6.8 million, respectively, which resulted from the recognition of development and regulatory milestones and amortization of the up-front payments under the collaboration agreement with Sumitomo Dainippon.

Cost of sales

Cost of sales was $1.4 million and $0 for the years ended December 31, 2017 and 2016, respectively, due to the commercial launch in the United States for Ocaliva in PBC in June 2016 and in certain European countries in 2017.

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 is primarily due to increased expenses of approximately $24.1 million in additional personnel-related costs to support our commercial and international initiatives, $9.8 million in expenses, which included a $7.8 million termination fee, related to the 55 Hudson Yard lease termination, and $17.4 million in Ocaliva commercialization activities and market research and indirect expenses (rent, travel and product-related legal costs) of $3.0 million. These increases were partially offset by the one-time net expense of $45.0 million attributable to the settlement of a purported securities class action lawsuit in 2016 plus related legal expenses of $3.4 million in 2016, along with a decrease in consultant spend of $5.8 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. This net increase in research and development expense primarily reflects an increase in OCA research and development activities of approximately $34.9 million to support our development activities, an increase of $2.2 million of compensation-related costs, and an increase of indirect costs of approximately $0.5 million.

Interest expense

Interest expense was $29.3 million and $14.2 million for the years ended December 31, 2017 and 2016, respectively, due to the issuance of our 3.25% convertible senior notes due 2023, or convertible notes, 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 is primarily attributable to interest income earned on cash, cash equivalents and investment securities, which increased compared to the prior year as a result of increases in cash and investment balances primarily due to the net proceeds from the issuance of our convertible notes.

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.

On December 22, 2017, the United States enacted tax reform legislation through the Tax Cuts and Jobs Act, which significantly changes the existing U.S. tax laws, including a reduction in the corporate tax rate to 21% and a move from a worldwide tax system to a territorial system, as well as other changes. As a result of the enactment of the legislation, we remeasured our deferred tax assets and liabilities, for which we continue to maintain a full valuation allowance as of December 31, 2017. Accordingly, there was no tax expense recorded in the consolidated financial statements as a result of adopting the legislation.

Comparison of the Years Ended December 31, 2016 and 2015

The following table summarizes our results of operations for the years ended December 31, 2016 and 2015, together with the changes in those items in dollars and as a percentage:

	Years Ended December 31,		Dollar Change	% Change
	2016	2015		
	(in thousands)			
Revenue:				
Product revenue, net	18,169	—	18,169	N/M
Licensing revenue	6,782	2,782	4,000	144%
Total revenue	24,951	2,782	22,169	797%
Operating expenses:				
Selling, general and administrative	273,596	119,242	154,354	129%
Research and development	153,893	112,696	41,197	37%
Total operating expenses	427,489	231,938	195,551	84%
Other income (expense):				
Interest expense	(14,196)	—	(14,196)	N/M
Other income, net	3,904	2,727	1,177	43%
Total other income (expense)	(10,292)	2,727	(13,019)	N/M
Net loss	$(412,830)	$(226,429)	$(186,401)	82%

* N/M = not meaningful.

Revenues

Product revenue, net was $18.2 million and $0 for the years ended December 31, 2016 and 2015, respectively. We commenced our commercial launch in the United States for Ocaliva in PBC in June 2016. For the years ended December 31, 2016 and 2015, licensing revenue was $6.8 million and $2.8 million, respectively, which resulted from the recognition of development and regulatory milestones and amortization of the up-front payments under the collaboration agreement with Sumitomo Dainippon.

Selling, general and administrative expenses

Selling, general and administrative expenses were $273.6 million and $119.2 million for the years ended December 31, 2016 and 2015, respectively. The $154.4 million net increase primarily reflects additional personnel-related costs of approximately $50.8 million to support our commercial and international initiatives, a one-time net expense of approximately $45.0 million attributable to the settlement of a purported securities class action lawsuit and increased expenses of approximately $27.5 million in market research and Ocaliva commercialization activities. Because of these initiatives, indirect expenses (rent, travel, and product related legal costs) and consultant spend increased by $19.1 million and $12.0 million, respectively.

Research and development expenses

Research and development expenses were $153.9 million and $112.7 million for the years ended December 31, 2016 and 2015, respectively, representing a net increase of $41.2 million. This net increase in research and development expense primarily reflects an increase in OCA research and development activities of approximately $38.6 million to support our development activities and an increase of $7.5 million of compensation-related costs, partially offset by a decrease of indirect costs of approximately $4.9 million.

Interest expense

Interest expense was $14.2 million and $0 for the years ended December 31, 2016 and 2015, respectively, due to the issuance of our 3.25% convertible senior notes due 2023, or convertible notes, in July 2016.

Other income, net

Other income, net was $3.9 million and $2.7 million for the years ended December 31, 2016 and 2015, respectively. The $1.2 million increase is primarily attributable to interest income earned on cash, cash

equivalents and investment securities, which increased compared to the prior year period as a result of increases in cash and investment balances primarily due to the net proceeds from the issuance of our convertible notes.

Income Taxes

For the years ended December 31, 2016 and 2015, 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.

Liquidity and Capital Resources

Sources of Liquidity

As of December 31, 2017, we had an accumulated deficit of $1.5 billion. We anticipate that we will continue to incur losses for at least the next several years. We expect that our research and development and selling, general and administrative expenses will continue to increase and, as a result, we will need additional capital to fund our operations, which we may seek to obtain through a combination of equity offerings, debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements.

We have funded our operations primarily through the sale of common stock, preferred stock, convertible notes and warrants and payments received under our collaboration agreements totaling approximately $1.4 billion (net of issuance costs of $46.1 million), including $29.7 million in net proceeds from our Series C financing in August 2012, $78.7 million in net proceeds from our initial public offering in October 2012, $61.2 million in net proceeds from our follow-on public offering in June 2013, $183.5 million in net proceeds from a follow-on public offering in April 2014, $191.6 million in net proceeds from a follow-on public offering in February 2015, $367.1 million in net proceeds from the follow-on offering in April 2015, $447.6 million in net proceeds from the issuance of the convertible notes in July 2016, and the receipt of $22.0 million in up-front payments and milestones under our licensing and collaboration agreements. As of December 31, 2017, we had cash, cash equivalents and investment securities of $414.9 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. Currently, our funds are held in cash and money market bank accounts and investments, all of which have maturities of less than two years.

Cash Flows

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

	Years Ended December 31,		
	2017	2016	2015
		(in thousands)	
Net cash provided by (used in):			
Operating activities	$(265,402)	$(342,441)	$ (162,902)
Investing activities	287,775	(60,135)	(389,472)
Financing activities	2,838	414,382	565,469
Effect of exchange rate changes	1,127	(873)	(376)
Net increase in cash and cash equivalents	$ 26,338	$ 10,933	$ 12,719

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

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

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

Net cash used in operating activities of $162.9 million for the year ended December 31, 2015 was primarily a result of our $226.4 million net loss partially offset by net changes in operating assets and liabilities of $21.3 million, $34.2 million for stock-based compensation, $1.7 million for depreciation and the amortization of investment premium of $6.3 million.

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

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

For the year ended December 31, 2015, net cash used in investing activities primarily reflects the purchase of investment securities of $640.7 million, partially offset by the sale of investment securities of $257.2 million to fund operations and expenditures for leasehold improvements of $5.9 million primarily for our King's Cross, London facility and the expansion of our New York headquarters.

Financing Activities. 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 the issuance of our convertible notes that occurred in July 2016 of $447.6 million, net of issuance cost, and $5.2 million from the exercise of options to purchase common stock, partially offset by payments of $38.4 million for the capped call transactions related to our convertible notes.

Net cash provided by financing activities in the year ended December 31, 2015 consisted primarily of net proceeds of the February 2015 public offering of $191.6 million, the April 2015 public offering of $367.2 million, and $6.7 million from the exercise of options to purchase common stock.

Future Funding Requirements

While we commenced our commercial launch of Ocaliva for use in PBC in the United States, Europe and other jurisdictions where it has received marketing approval, we cannot predict the period, if any, in which material net cash inflows from sales of OCA or our other product candidates can sustain our operations. We expect to continue to incur significant expenses in connection with our ongoing development activities, particularly as we continue the research, development and clinical trials of, and seek regulatory approval for, our product candidates.

We have incurred and expect to incur additional costs associated with our plans to further expand our operations in the United States, Europe and in certain other countries. In addition, subject to obtaining regulatory approval of any of our product candidates, we expect to incur significant commercialization expenses for product sales, marketing, manufacturing and distribution. As part of our longer-term strategy, we also anticipate incurring expenses in connection with increases in our product development, scientific, commercial and administrative personnel and expansion of our infrastructure in the United States and abroad. We may also engage in activities that involve potential in- or out-licensing of products or technologies or acquisitions of other products, technologies or businesses. We anticipate that we will need substantial additional funding in connection with our continuing operations.

Adjusted operating expense is a financial measure not calculated in accordance with GAAP. We anticipate that stock-based compensation expense will represent the most significant non-cash item that is excluded from adjusted operating expenses as compared to operating expenses under GAAP. For the year ended December 31, 2016, adjusted operating expense also excludes a one-time $45 million net expense for the settlement of a purported class action lawsuit. See Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operation" — "Non-GAAP Financial Measures" for more information.

Due to the many variables inherent to the development and commercialization of novel therapies and our rapid growth and expansion, we currently cannot accurately and precisely predict the duration beyond mid-2019 over which we expect our cash and cash equivalents to be sufficient to fund our operating expenses and capital expenditure requirements. However, we currently believe that our cash and cash equivalents will be sufficient for us to:

- continue the initial commercialization of Ocaliva for PBC in the United States, the European Union and other jurisdictions where it has received marketing approval;
- prepare for and initiate the commercial launch of Ocaliva in PBC in certain other target markets across the world, but not commercially launch Ocaliva in PBC in non-target countries across the world;
- continue and expand our clinical development programs for OCA in PBC and NASH, such as continuing, but not completing, our planned Phase 3 clinical program for OCA in NASH, including the REGENERATE trial, and our ongoing COBALT confirmatory clinical outcomes trial of OCA in PBC; and
- conduct further assessments of OCA for use in PSC and potentially initiate, but not complete, additional clinical trials for OCA in PSC.

Accordingly, we will continue to require substantial additional capital in connection with our continuing operations, including continuing our commercialization plans and our research and development activities and building our global infrastructure to support these activities.

The amount and timing of our future funding requirements will depend on many factors, including:

- the rate of progress and cost of our continued commercialization activities for Ocaliva in PBC in jurisdictions where it has received marketing approval;
- our ability to receive marketing approval of Ocaliva for PBC in countries where it has not received marketing approval based on our regulatory submissions package and our work completed to date, including the willingness of the relevant regulatory authorities to accept the POISE trial, which is our completed Phase 3 clinical trial for PBC;
- the degree of effort and time needed to prepare for and initiate the commercial launches of Ocaliva in PBC in the jurisdictions where it receives marketing approval;
- the progress, costs, results of and timing of our clinical development programs for OCA in PBC, NASH, PSC and other indications, such as the COBALT trial, the REGENERATE trial, the ongoing Phase 3 trial in NASH patients with cirrhosis or other trials we may conduct;
- the outcome, costs and timing of seeking and obtaining FDA, EMA and any other regulatory approvals;
- the expansion of our research and development activities and the product candidates that we pursue, including our product candidates in preclinical development such as INT-777;
- the expansion of our operations, personnel and the size of our company and our need to continue to expand in the longer term;
- the costs associated with securing and establishing manufacturing capabilities and procuring the materials necessary for our products and product candidates;
- market acceptance of our products and product candidates, which may be affected by reimbursement from payors;
- the costs of acquiring, licensing or investing in businesses, products, product candidates and technologies;

- our ability to maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights;
- the effect of competing technological and market developments; and
- other cash needs that may arise as we continue to operate our business.

We have no committed external sources of funding. Until such time, if ever, as we can consistently generate profits from our operations and become profitable, we expect to finance our cash needs through a combination of equity offerings, debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our common stockholders 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. If we raise additional funds through government or other third-party funding, marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

Non-GAAP Financial Measures

This Annual Report presents projected adjusted operating expense, which is a financial measure not calculated in accordance with U.S. generally accepted accounting principles, or GAAP, and should be considered in addition to, but not as a substitute for, operating expense that we prepare and announce in accordance with GAAP. We exclude certain items from adjusted operating expense, such as stock-based compensation and other non-cash items, that management does not believe affect our basic operations and that do not meet the GAAP definition of unusual or non-recurring items. For the year ended December 31, 2016, adjusted operating expense also excludes a one-time $45 million net expense for the settlement of a purported class action lawsuit. Other than the net class action lawsuit settlement amount, which is a one-time expense, we anticipate that stock-based compensation expense will represent the most significant non-cash item that is excluded in adjusted operating expenses as compared to operating expenses under GAAP. A reconciliation of projected non-GAAP adjusted operating expense to operating expense calculated in accordance with GAAP is not available on a forward-looking basis without unreasonable effort due to an inability to make accurate projections and estimates related to certain information needed to calculate, for example, future stock-based compensation expense. Management also uses adjusted operating expense to establish budgets and operational goals and to manage our company's business. Other companies may define this measure in different ways. We believe this presentation provides investors and management with supplemental information relating to operating performance and trends that facilitate comparisons between periods and with respect to projected information.

As of December 31, 2017, we had $414.9 million in cash, cash equivalents and investment securities. We currently project adjusted operating expenses in the range of $390 million to $410 million in the fiscal year ending December 31, 2018, which excludes stock-based compensation and other non-cash items. These expenses are planned to support the continued commercialization of Ocaliva in PBC in the United States and other markets, the continued clinical development for OCA in PBC and NASH and PSC and our other earlier stage pipeline programs. We may make additional investments over 2018 as our business evolves.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which we have prepared in accordance with GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenues and expenses during the reporting periods. 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 may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 3 to our consolidated financial statements appearing elsewhere in this Annual Report, 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

Product Revenue, Net

Revenue is recognized when the four basic criteria of revenue recognition are met: (1) persuasive evidence that an arrangement exists; (2) delivery has occurred or services have been rendered; (3) the fee is fixed or determinable; and (4) collectability is reasonably assured. When the revenue recognition criteria are not met, we defer the recognition of revenue by recording deferred revenue on the balance sheet until such time that all criteria are met.

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 the treatment of PBC and the Company commenced launch in January of 2017. In May 2017, Health Canada granted a conditional approval for the treatment of PBC and the Company commenced launch in July of 2017. 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 recognized net sales of Ocaliva of $18.2 million for the year ended December 31, 2016. The Company also recorded $3.9 million in deferred revenues recorded in short-term portion of deferred revenue on its balance sheet, which represents product shipped to distributors, but not sold through as of December 31, 2016.

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 now believes it has accumulated sufficient data to reasonably estimate product returns and, therefore, it will now effectively 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 nine months ended September 30, 2017. The Company also established a new reserve of $0.7 million during the third quarter of 2017 related to future returns from its customers under its various contracts.

The Company has written contracts with each of its customers and delivery occurs when the customer receives Ocaliva. The Company evaluates the creditworthiness of each of its customers to determine whether collection is reasonably assured. In order to conclude that the price is fixed and determinable, the Company must be able to (i) calculate its gross product revenues from the sales to its customers and (ii) reasonably estimate its net product revenues. The Company calculates gross product revenues based on the wholesale acquisition cost that the Company charges its customers for Ocaliva. The Company estimates its net product revenues by deducting from its gross product revenues (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, or CMS, 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 accrued liabilities on the condensed consolidated balance sheet.

Other Incentives

Other incentives that we offer to indirect customers include co-pay assistance cards provided for PBC patients whom 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 each period 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 accrued liabilities on the condensed consolidated balance sheet.

Valuation of Stock-Based Compensation

We record the fair value of stock options, restricted stock units, or RSUs, and restricted stock awards, or RSAs, issued to employees as of the grant date as compensation expense. We recognize compensation expense over the requisite service period, which is generally the vesting period. For non-employees, we also record stock options, RSUs and RSAs at their fair value as of the grant date. We then periodically re-measure the awards to reflect the current fair value at each reporting period until the non-employee completes the performance obligation or the date on which a performance commitment is reached. Expense is recognized over the related service period.

We calculate the fair value of stock-options using the Black-Scholes option-pricing model. The Black-Scholes option-pricing model requires the use of assumptions, including stock price volatility, the expected life of stock options, risk free interest rate and the fair value of the underlying common stock on the date of grant. Our key assumptions are:

- The expected volatility was estimated based upon the historical volatility information of peer companies for each respective reporting period. We calculated expected volatility based on reported data for selected reasonably similar publicly traded companies for which the historical information is available. 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.
- We determine the risk-free interest rate by reference to implied yields available from U.S. Treasury securities with a remaining term equal to the expected life assumed at the date of grant.
- We account for forfeitures as they occur.

We expect the impact of stock-based compensation may fluctuate in future periods due to the potential changes in the value of our common stock, changes to our headcount and the award of additional stock option and other equity grants to our personnel.

Convertible Senior Notes and Capped Call Transactions

In July 2016, we completed an underwritten public offering of $460.0 million in the aggregate principal amount of 3.25% convertible senior notes due in 2023, or the Convertible Notes. After deducting the underwriting discounts and offering expenses of approximately $12.4 million, the net proceeds from the Convertible Notes offering were approximately $447.6 million. In connection with the offering, we entered into an indenture, as supplemented by the First Supplemental Indenture relating to the Convertible Notes, or, collectively, the Indenture, with U.S. Bank National Association, a national banking association, as trustee governing the Convertible Notes. The Convertible Notes bear interest at a rate of 3.25% per annum, payable semi-annually on January 1 and July 1 of each year, beginning on January 1, 2017. The Convertible Notes mature on July 1, 2023, unless earlier repurchased, redeemed or converted. Holders may convert the 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: (1) during any calendar quarter (and only during such calendar quarter) commencing after the calendar quarter ending on September 30, 2016, if the last reported sale price of our common stock for at least 20 trading days (whether or not consecutive) during a 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; (2) during the five business day period after any five consecutive trading day period, or the measurement period, in which the trading price (as defined in the Indenture) per $1,000 principal amount of convertible notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of our common stock and the conversion rate on each such trading day; (3) if we call 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 (4) 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, we will pay or deliver, as the case may be, cash, shares of our common stock (and cash in lieu of any fractional shares) or a combination of cash and shares of our common stock, at our election. The conversion rate will initially be 5.0358 shares of our common stock per $1,000 principal amount of convertible notes (equivalent to an initial conversion price of approximately $198.58 per share of common stock). The conversion rate will be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. In addition, following certain corporate events that occur prior to the maturity date, we will increase the conversion rate for a holder who elects to convert its convertible notes in connection with such a corporate event in certain circumstances.

We may not redeem the Convertible Notes prior to July 6, 2021. We may redeem for cash all or any portion of the Convertible Notes, at our option, on or after July 6, 2021, if the last reported sale price of our 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 we provide 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. No sinking fund is provided for the Convertible Notes.

If we undergo a fundamental change, 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.

The Convertible Notes are our senior unsecured obligations and rank senior in right of payment to our future indebtedness that is expressly subordinated in right of payment to the Convertible Notes; equal in right of payment to our future unsecured indebtedness that is not so subordinated; effectively junior in right of payment to our future secured indebtedness to the extent of the value of the assets securing such indebtedness; and structurally subordinated to all existing and future indebtedness and other liabilities (including trade payables) incurred by our subsidiaries.

The Indenture contains customary events of default with respect to the Convertible Notes, including that upon certain events of default occurring and continuing, the trustee by notice to us, or the holders of at least

25% in principal amount of the outstanding convertible notes by notice to us, may (subject to the provisions of the Indenture) declare 100% of the principal of and accrued and unpaid interest, if any, on all the Convertible Notes to be due and payable. In case of certain events of bankruptcy, insolvency or reorganization involving us or a significant subsidiary, 100% of the principal of and accrued and unpaid interest on the Convertible Notes will automatically become due and payable. Upon such a declaration of acceleration, such principal and accrued and unpaid interest, if any, will be due and payable immediately.

In connection with the pricing of the Convertible Notes, we entered into privately-negotiated capped call transactions with Royal Bank of Canada, or RBC, UBS AG, London Branch, or UBS, and Credit Suisse Capital LLC, or Credit Suisse. The aggregate cost of the capped call transactions entered into in connection with the pricing of the notes was approximately $33.4 million. We and RBC, UBS and Credit Suisse entered into additional capped call transactions in connection with the underwriters' exercise of their over-allotment option in full at an aggregate cost of approximately $5.0 million. The capped call transactions are generally expected to reduce the potential dilution 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 will initially be $262.27 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 upon conversion of the Convertible Notes to the extent that such market price exceeds the cap price of the capped call transactions.

Income Taxes

No income tax expense or benefit was recognized in the accompanying consolidated financial statements. 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.

Contractual Obligations and Commitments

Our long-term contractual obligations include commitments and estimated purchase obligations entered into in the normal course of business. The following table summarizes our significant contractual obligations and commercial commitments as of December 31, 2017 and the effects such obligations are expected to have on our liquidity and cash flows in future periods:

	Payments Due By Period				
	Total	Less than 1 year	1 – 3 years	4 – 5 years	More than 5 years
			(in thousands)		
Operating leases	$ 30,377	$ 7,602	$ 12,315	$ 6,525	$ 3,935
Long-term debt	460,000	—	—	—	460,000
Purchase obligations	40,230	27,332	9,206	3,016	676
Total	$ 530,607	$ 34,934	$ 21,521	$ 9,541	$ 464,611

See Item 2. "Properties" to this Annual Report for a description of our operating leases. In addition to the general description of our operating leases, the following provides additional details related to our leases for the Hudson Yards development.

In December 2017, we terminated the lease agreement relating to 55 Hudson Yards and have chosen to stay in our current 10 Hudson Yards location in order to reduce our long-term lease obligations. We incurred $9.8 million in expenses, which included a $7.8 million termination fee. In addition, we also reduced our future operating lease obligation by $124.5 million over the life of that lease.

See "— Critical Accounting Policies and Estimates — Convertible Senior Notes and Capped Call Transactions" above for a description of our convertible notes.

We are a party to license and research and development agreements with universities and other third parties, as well as patent assignment agreements, under which we have obtained rights to patents, patent applications and know-how. We enter into contracts in the normal course of business with CRO, for clinical trials, clinical and commercial supply manufacturing, with vendors for commercial and precommercial activities, research and development activities and other services and products for operating purposes. Our agreements generally provide for termination within 90 days of notice. Such agreements are cancelable contracts and not included in the table of contractual obligations and commitments. We have included as purchase obligations our commitments under agreements to the extent they are quantifiable and are not cancelable.

Under our agreement with Sumitomo Dainippon, we are required to use our commercially reasonable efforts to develop OCA outside of the territories in which Sumitomo Dainippon has a license under the agreement. As these amounts are not quantifiable, they are not included in the table above.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements as defined under Securities and Exchange Commission rules.

Recent Accounting Pronouncements

See Note 3 to the consolidated financial statements for a full description of recent accounting pronouncements including the respective expected dates of adoption and expected effects on results of operations and financial condition.

Basic and Diluted Net Loss Attributable to Common Stockholders per Share of Common Stock

Our Series A, B and C preferred stock represented participating securities. However, since we have operated at a loss since inception, and losses are not allocated to the preferred stock, the two class method did not affect our calculation of earnings per share. Upon the closing of our initial public offering, all outstanding shares of our preferred stock were converted into an aggregate of 7,403,817 shares of common stock.

Dilutive common stock equivalents would include the dilutive effect of convertible securities, common stock options, RSUs, RSAs and warrants to purchase common stock. Potentially dilutive common stock equivalents totaled approximately 2.3 million shares, 1.9 million shares, and 1.5 million shares for the years ended December 31, 2017, 2016 and 2015, respectively. Potentially dilutive common stock equivalents were excluded from the diluted earnings per share denominator for all periods because of their anti-dilutive effect. Therefore, the weighted average shares used to calculate both basic and diluted earnings per share are the same.

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 securities, we do not believe that an increase in market rates would have any significant impact on the realized value of our investment securities. If a 10% change in interest rates were to have occurred on December 31, 2017, 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 2017, 2016 or 2015.

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. An index of those financial statements is found in Item 15.

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 principal executive officer and principal financial officer evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2017. 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 Securities and Exchange Commission'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. In designing and evaluating our disclosure controls and procedures, our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and our 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, 2017, our principal executive officer and principal financial officer concluded that, as of such date, our disclosure controls and procedures were adequate and effective.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting for our company. Internal control over financial reporting is defined in Rule 13a-15(f) or 15d-15(f) promulgated 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 GAAP 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.

Internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements prepared for external purposes in accordance with generally accepted accounting principles. 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 principal executive officer and principal financial officer, assessed the effectiveness of our internal control over financial reporting as of December 31, 2017. In making this assessment, our management used the criteria set forth in the Internal Control — Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on its assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2017 based on those criteria.

Attestation Report of Independent Registered Public Accounting Firm

The effectiveness of our internal control over financial reporting as of December 31, 2017 has been audited by KPMG LLP, an independent registered public accounting firm, as stated in their report which is included in this Annual Report.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act), identified in connection with the evaluation of such internal control, that occurred during the three months ended December 31, 2017 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

Pursuant to Paragraph G(3) of the General Instructions to Form 10-K, the information required by Part III (Items 10, 11, 12, 13, and 14) is being incorporated by reference herein to our definitive proxy statement to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2017 in conjunction with our 2018 Annual Meeting of Stockholders.

Item 11. Executive Compensation

See Item 10.

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

See Item 10.

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

See Item 10.

Item 14. Principal Accounting Fees and Services

See Item 10.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) The following documents are filed as part of this Annual Report:

(1) Financial Statements:

(2) Financial Statement Schedules:

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(3) Exhibits. The exhibits filed as part of this Annual Report are set forth on the Exhibit Index immediately below.

Item 16. Form 10-K Summary

None.

SIGNATURES

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

INTERCEPT PHARMACEUTICALS, INC.

Date: February 28, 2018

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

Date: February 28, 2018

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

Pursuant to the requirements of the Exchange Act, this Annual Report has been signed by the following persons in the capacities indicated below and on the dates indicated:

Signature	Title	Date
/s/ Mark Pruzanski, M.D. Mark Pruzanski, M.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	February 28, 2018
/s/ Sandip Kapadia Sandip Kapadia	Chief Financial Officer (Principal Financial and Accounting Officer)	February 28, 2018
/s/ Paolo Fundarò Paolo Fundarò	Chairman of the Board of Directors	February 28, 2018
/s/ Srinivas Akkaraju, M.D., Ph.D. Srinivas Akkaraju, M.D., Ph.D.	Director	February 28, 2018
/s/ Luca Benatti, Ph.D. Luca Benatti, Ph.D.	Director	February 28, 2018
/s/ Daniel Bradbury Daniel Bradbury	Director	February 28, 2018
/s/ Keith Gottesdiener, M.D. Keith Gottesdiener, M.D.	Director	February 28, 2018
/s/ Gino Santini Gino Santini	Director	February 28, 2018
/s/ Glenn Sblendorio Glenn Sblendorio	Director	February 28, 2018
/s/ Daniel Welch Daniel Welch	Director	February 28, 2018

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, 2017 and 2016, 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, 2017, 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, 2017 and 2016, and the results of its operations and its cash flows for each of the years in the three year period ended December 31, 2017, 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, 2017, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO), and our report dated February 28, 2018 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
February 28, 2018

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, 2017, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2017, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

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, 2017 and 2016, 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, 2017, and the related notes (collectively, the "consolidated financial statements"), and our report dated February 28, 2018 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
February 28, 2018

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Balance Sheets

	December 31, 2017	December 31, 2016
	(in thousands)	
Assets		
Current assets:		
Cash and cash equivalents	$ 70,013	$ 43,675
Investment securities, available-for-sale	344,904	645,710
Accounts receivable	16,501	9,126
Prepaid expenses and other current assets	16,889	9,354
Total current assets	448,307	707,865
Fixed assets, net	16,184	11,295
Inventory	3,480	2,279
Security deposits	16,376	17,814
Total assets	$ 484,347	$ 739,253
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable, accrued expenses and other liabilities	$ 94,777	$ 65,551
Short-term interest payable	7,475	7,267
Short-term portion of deferred revenue	1,782	5,694
Total current liabilities	104,034	78,512
Long-term liabilities:		
Long-term debt	355,677	341,356
Long-term other liabilities	5,578	—
Long-term portion of deferred revenue	2,672	4,453
Total liabilities	$ 467,961	$ 424,321
Stockholders' equity:		
Common stock par value $0.001 per share; 45,000,000 shares authorized; 25,172,678 and 24,819,918 shares issued and outstanding as of December 31, 2017 and December 31, 2016, respectively	25	25
Additional paid-in capital	1,486,690	1,426,168
Accumulated other comprehensive loss, net	(786)	(2,801)
Accumulated deficit	(1,469,543)	(1,108,460)
Total stockholders' equity	16,386	314,932
Total liabilities and stockholders' equity	$ 484,347	$ 739,253

See accompanying notes to consolidated financial statements.

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Statements of Operations

	Years Ended December 31,		
	2017	2016	2015
	(in thousands, except per share data)		
Revenue:			
Product revenue, net	$ 129,175	$ 18,169	$ —
Licensing revenue	1,781	6,782	2,782
Total revenue	130,956	24,951	2,782
Operating expenses:			
Cost of sales	1,371	—	—
Selling, general and administrative	273,698	273,596	119,242
Research and development	191,499	153,893	112,696
Total operating expenses	466,568	427,489	231,938
Operating loss	(335,612)	(402,538)	(229,156)
Other income (expense):			
Interest expense	(29,271)	(14,196)	—
Other income, net	4,516	3,904	2,727
Total other income (expense)	(24,755)	(10,292)	2,727
Net loss	$(360,367)	$(412,830)	$ (226,429)
Net loss per common and potential common share:			
Basic and diluted	$ (14.38)	$ (16.74)	$ (9.56)
Weighted average common and potential common shares outstanding:			
Basic and diluted	25,054	24,663	23,694

See accompanying notes to consolidated financial statements.

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Statements of Comprehensive Loss

	Years Ended December 31,		
	2017	2016	2015
		(in thousands)	
Net loss	$(360,367)	$(412,830)	$(226,429)
Other comprehensive loss:			
Unrealized gains (losses) on securities:			
Unrealized holding gains (losses) arising during the period	791	378	(1,628)
Reclassification for recognized gains (losses) on marketable investment securities during the period recognized in other income, net of tax	—	(48)	3
Net unrealized gains (losses) on marketable investment securities	$ 791	$ 330	$ (1,625)
Foreign currency translation adjustments	1,225	(878)	(347)
Comprehensive loss	$(358,351)	$(413,378)	$(228,401)

See accompanying notes to consolidated financial statements.

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Statements of Changes in Stockholders' Equity
For the Years Ended December 31, 2017, 2016, and 2015
(in thousands)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Stockholders' Equity (Deficit)
	Shares	Amount				
Balance – December 31, 2014	21,416	$ 22	$ 700,355	$ (469,201)	$ (281)	$ 230,895
Stock-based compensation	—	—	34,189	—	—	34,189
Issuance of common stock from public offering, net of underwriting fees and issuance costs	2,481	1	558,753	—	—	558,754
Net proceeds from exercise of stock options	495	1	6,711	—	—	6,712
Other comprehensive loss	—	—	—	—	(1,972)	(1,972)
Net loss	—	—	—	(226,429)	—	(226,429)
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

See accompanying notes to consolidated financial statements.

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Statements of Cash Flows

	Years Ended December 31,		
	2017	2016	2015
		(in thousands)	
Cash flows from operating activities:			
Net loss	$(360,367)	$(412,830)	$ (226,429)
Adjustments to reconcile net loss to net cash used in operating activities:			
Share-based compensation	56,968	46,205	34,189
Amortization of investment premium	3,429	4,939	6,302
Amortization of deferred financing costs	1,417	685	—
Realized loss on investments	—	48	—
Depreciation	4,601	3,831	1,691
Loss on the disposal of property and equipment	1,000	—	—
Accretion of debt discount	12,904	6,242	—
Changes in operating assets:			
Prepaid expenses and other current assets	(7,535)	4,284	(7,516)
Security deposits	1,438	(13,796)	(1,575)
Accounts receivable	(7,375)	(9,126)	—
Inventory	(1,201)	(2,279)	—
Changes in operating liabilities:			
Accounts payable, accrued expenses and other current liabilities	29,226	19,960	32,218
Interest payable	208	7,267	—
Long-term other liabilities	5,578	—	—
Deferred revenue	(5,693)	2,129	(1,782)
Net cash used in operating activities	(265,402)	(342,441)	(162,902)
Cash flows from investing activities:			
Purchases of investment securities	(231,107)	(511,521)	(640,709)
Sales of investment securities	529,274	456,465	257,172
Purchases of equipment, leasehold improvements, and furniture and fixtures	(10,392)	(5,079)	(5,935)
Net cash provided by (used in) investing activities	287,775	(60,135)	(389,472)
Cash flows from financing activities:			
Proceeds from issuance of stock offerings, net of issuance costs	—	—	558,756
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	2,838	5,173	6,713
Net cash provided by financing activities	2,838	414,382	565,469
Effect of exchange rate changes	1,127	(873)	(376)
Net increase in cash and cash equivalents	26,338	10,933	12,719
Cash and cash equivalents – beginning of period	43,675	32,742	20,023
Cash and cash equivalents – end of period	$ 70,013	$ 43,675	$ 32,742

See accompanying notes to consolidated financial statements.

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Overview of Business

Intercept Pharmaceuticals, Inc. ("Intercept" or the "Company") is a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat non-viral, progressive liver diseases, including primary biliary cholangitis ("PBC"), nonalcoholic steatohepatitis ("NASH"), primary sclerosing cholangitis ("PSC") and biliary atresia. Founded in 2002 in New York, Intercept now has operations in the United States, Europe and Canada.

2. Basis of Presentation

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 preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent 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 those estimates.

3. Summary of Significant Accounting Policies

Principles of Consolidation

The consolidated financial statements include the accounts of Intercept 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.

Cash and Cash Equivalents

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

Investment Securities, Available for Sale

Investment 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 securities classified as available-for-sale is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion are included in interest income. 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 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, uncertainties related to commercialization of products, and regulatory approval.

Concentration of Credit Risk

Financial instruments, which potentially subject the Company to concentrations of credit risk, principally consist of cash, cash equivalents and investment 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

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies – (continued)

principal and liquidity. 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. On a consolidated basis, for the year ended December 31, 2016, the Company's three largest customers accounted for 49%, 37% and 12%, 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 $16.5 million and $9.1 million of accounts receivable as of December 31, 2017 and 2016, respectively, and has not recorded an allowance for any doubtful accounts as of December 31, 2017 and 2016. 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. On a consolidated basis, the Company's three largest customers accounted for 45%, 38% and 14% of the December 31, 2016 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.

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 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.

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") 470, formerly FSP APB 14-1, Accounting for Convertible Debt Instruments That May be Settled in

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies – (continued)

Cash upon Conversion (Including Partial Cash Settlement). 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 these 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 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 10 — Long-Term Debt.

Revenue Recognition

Product Revenue, Net

Revenue is recognized when the four basic criteria of revenue recognition are met: (1) persuasive evidence that an arrangement exists; (2) delivery has occurred or services have been rendered; (3) the fee is fixed or determinable; and (4) collectability is reasonably assured. When the revenue recognition criteria are not met, we defer the recognition of revenue by recording deferred revenue on the balance sheet until such time that all criteria are met.

The Company commenced its commercial launch of Ocaliva® (obeticholic acid or "OCA") for the treatment of PBC in the United States in June 2016. In December 2016, the European Commission granted conditional approval for the treatment of PBC and the Company commenced launch in January of 2017. In May 2017, Health Canada granted a conditional approval for the treatment of PBC and the Company commenced launch in July of 2017. 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 recognized net sales of Ocaliva of $18.2 million for the year ended December 31, 2016. The Company also recorded $3.9 million in deferred revenues recorded in short-term portion of deferred revenue on its balance sheet, which represents product shipped to distributors, but not sold through as of December 31, 2016.

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 now believes it has accumulated sufficient data to reasonably estimate product returns and, therefore, it will now effectively 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 nine months ended September 30, 2017. The Company also established a new reserve of $0.7 million during the third quarter of 2017 related to future returns from its customers under its various contracts.

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies – (continued)

The Company has written contracts with each of its customers and delivery occurs when the customer receives Ocaliva. The Company evaluates the creditworthiness of each of its customers to determine whether collection is reasonably assured. In order to conclude that the price is fixed and determinable, the Company must be able to (i) calculate its gross product revenues from the sales to its customers and (ii) reasonably estimate its net product revenues. The Company calculates gross product revenues based on the wholesale acquisition cost that the Company charges its customers for Ocaliva. The Company estimates its net product revenues by deducting from its gross product revenues (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

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 Centers for Medicare & Medicaid Services ("CMS") 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 accrued 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 whom 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 each period 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 accrued liabilities on the consolidated balance sheet.

Licensing Revenue

The Company accounts for the development, regulatory and sales milestones within an arrangement in accordance with the milestone method of revenue recognition. This method allows for the recognition of consideration which is contingent on the achievement of a substantive milestone in its entirety in the period the milestone is achieved. Each future milestone is considered substantive if it: (i) relates solely to the past performance of the intellectual property to achieve the milestone; (ii) is reasonable relative to all of the deliverables and payment terms in the arrangement; and (iii) is commensurate with either the Company's performance or the enhanced value of the intellectual property as a result of a specific outcome resulting from the Company's performance.

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 obeticholic acid ("OCA"). For periods prior to the commercial launch of Ocaliva in

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies – (continued)

PBC in June 2016, the manufacturing costs for OCA were expensed as part of research and development. The Company will continue to incur manufacturing costs for commercial supply of OCA in other indications such as NASH prior to their approval.

Stock-based Compensation

The Company accounts for stock-based compensation in accordance with Financial Accounting Standards Board's Accounting Standards Codification ("ASC") 718, "Compensation — Stock Compensation" (ASC 718). The Company estimates the fair value of stock options using the Black-Scholes option pricing model on the date of the grant. Restricted stock units and restricted stock awards are valued based on the closing price of the Company's common stock on the date of the grant. The fair value of equity instruments expected to vest after taking into consideration an estimate of award forfeitures based on actual experience are recognized and amortized on a straight-line basis over the requisite service period of the award. Generally stock options fully vest four years from the grant date and have a term of ten years. The Company recognizes stock-based compensation for consultants 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 stock options and restricted stock units ("RSUs") 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, 2017 and 2016, 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, 2017 and 2016, the Company had no reserves for unrecognized tax benefits.

Segments

The Company operates in one segment. The Company is a biopharmaceutical company focused on discovering, developing and commercializing treatments for non-viral, progressive liver diseases.

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies – (continued)

Recent Accounting Pronouncements

In May 2014, the FASB issued ASU No. 2014-09, "Revenue from Contracts with Customers (Topic 606)" (ASU 2014-09), and subsequently issued modifications or clarifications in ASU No. 2015-14, "Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date," ASU 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 either using 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 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. As of the third quarter of 2017, the Company concluded that it had accumulated sufficient data to reasonably estimate product returns and, therefore, it began recognizing 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 the third quarter of 2017 related to future returns from its customers under its various contracts. Because the Company changed its revenue recognition polices to the sell-in basis during the third quarter of 2017, the adoption of ASU 2014-09 did not result in an adjustment to amounts previously recognized as revenue under Topic 605, and there were no other significant changes impacting the timing or measurement of our revenue or our business processes and controls.

On August 27, 2014, the FASB issued ASU 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern ("ASU 2014-15"), which requires an entity to evaluate whether conditions or events, in the aggregate, raise substantial doubt about the entity's ability to continue as a going concern for one year from the date the financial statements are issued or are available to be issued. The guidance became effective January 1, 2017. The Company adopted ASU No. 2014-15 on January 1, 2017, and its adoption did not have a material impact on the Company's financial statements.

In January 2016, FASB issued ASU 2016-01, 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

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies – (continued)

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 is currently evaluating the impact that the adoption of ASU 2016-01 will have on its consolidated financial statements and related disclosures, but does not expect it to have a significant impact.

In February 2016, the FASB issued ASU 2016-02, Leases ("ASU 2016-02") which supersedes Topic 840, Leases. ASU 2016-02 requires lessees to recognize a right-of-use asset and a lease liability on their balance sheets for all the leases with terms greater than twelve months. Based on certain criteria, leases will be classified as either financing or operating, with classification affecting the pattern of expense recognition in the income statement. For leases with a term of twelve months or less, a lessee is permitted to make an accounting policy election by class of underlying asset not to recognize lease assets and lease liabilities. If a lessee makes this election, it should recognize lease expense for such leases generally on a straight-line basis over the lease term. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018, and interim periods within those years, with early adoption permitted. In transition, lessees and lessors are required to recognize and measure leases at the beginning of the earliest period presented using a modified retrospective approach. The modified retrospective approach includes a number of optional practical expedients primarily focused on leases that commenced before the effective date of Topic 842, including continuing to account for leases that commence before the effective date in accordance with previous guidance, unless the lease is modified. The Company is evaluating the impact of the adoption of the standard on its consolidated financial statements and related disclosures.

In March 2016, the FASB issued ASU 2016-09, Improvements to Employee Share-Based Payment Accounting ("ASU 2016-09") which is intended to improve the accounting for share-based payment transactions as part of the FASB's simplification initiative. The ASU changes certain aspects of the accounting for share-based payment award transactions, including: (1) accounting for income taxes; (2) classification of excess tax benefits on the statement of cash flows; (3) forfeitures; (4) minimum statutory tax withholding requirements; and (5) classification of employee taxes paid on the statement of cash flows when an employer withholds shares for tax withholding purposes. The ASU is effective for fiscal years beginning after December 15, 2016, and interim periods within those years for public business entities. The Company adopted ASU 2016-09 during the first quarter of 2017. In connection with the adoption of this ASU, the Company elected to account for forfeitures as they occur and applied this change in accounting policy on a modified retrospective basis. As a result, the Company recorded a cumulative-effect adjustment to retained earnings which resulted in an increase to accumulated deficit of $0.7 million with an offsetting increase to additional paid-in capital (zero net total equity impact) as of the date of adoption, related to additional stock compensation expense that would have been recognized on unvested outstanding options unadjusted for estimated forfeitures. As a result of this guidance, the Company also recorded $58.7 million of additional deferred tax assets, which are fully offset by a valuation allowance. Other provisions of ASU 2016-09 had no impact on the Company's consolidated financial statements.

In May 2017, the FASB issued ASU 2017-09, Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting, which clarifies when to account for a change to the terms or conditions of a share-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 is evaluating the impact of adoption of the standard on the consolidated financial statements and related disclosures, but does not expect it to have a significant impact.

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies – (continued)

In July 2017, the FASB issued ASU 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 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 is currently assessing the potential impact of adopting ASU 2017-11 on its financial statements and related disclosures, but does not expect it to have a significant impact.

4. Significant Agreements

Sumitomo Dainippon Pharma Co., Ltd. (Sumitomo Dainippon)

In March 2011, the Company entered into an exclusive license agreement with Sumitomo Dainippon, under which the Company granted Sumitomo Dainippon an exclusive license to research, develop and commercialize OCA as a therapeutic for the treatment of PBC and NASH in Japan and China (excluding Taiwan). Under the terms of the license agreement, the Company received an up-front payment from Sumitomo Dainippon of $15.0 million and may be eligible to receive additional milestone payments of up to an aggregate of approximately $4 million in development milestones based on the initiation or completion of clinical trials, $19 million in regulatory approval milestones and tiered royalty payments up to the mid-twenties in percentage terms based on net sales of OCA products in China. As of December 31, 2017, the Company had achieved $6.0 million of the development milestones under its collaboration agreement with Sumitomo Dainippon. In May 2014, Sumitomo Dainippon exercised its option under the license agreement to add Korea as part of its licensed territories and paid the Company a $1.0 million up-front fee. Sumitomo Dainippon will be responsible for the costs of developing and commercializing OCA in its territories.

The Company evaluated the license agreement with Sumitomo Dainippon and determined that it is a revenue arrangement with multiple deliverables, or performance obligations. The Company's substantive performance obligations under this license 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. This development period is currently estimated as continuing through June 2020 and, as such, the up-front payment and payments made in respect of the Korea option are being recognized ratably over this period. During the years ended December 31, 2017 and 2016, the Company recorded revenue of approximately $1.8 million and $6.8 million, respectively.

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

5. Cash, Cash Equivalents, and Investments

The following table summarizes the Company's cash, cash equivalents and investments as of December 31, 2017 and December 31, 2016:

	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
Investments:				
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, 2016			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
	(in thousands)			
Cash and cash equivalents:				
Cash and money market funds	$ 43,675	$ —	$ —	$ 43,675
Investments:				
Commercial paper	66,185	—	(71)	66,114
Corporate debt securities	554,847	14	(1,443)	553,418
U.S. government and agency securities	26,254	—	(76)	26,178
Total investments	647,286	14	(1,590)	645,710
Total cash, cash equivalents and investments	$ 690,961	$ 14	$ (1,590)	$ 689,385

As of December 31, 2017, the Company held a total of forty-one positions that were in a continuous unrealized loss position for more than twelve months. The Company has determined that the unrealized losses are deemed to be temporary impairments as of December 31, 2017. 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, 2017.

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

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

The fair value for the Company's available-for-sale investments, which have been in an unrealized loss position for less than and longer than 12 months is as follows:

	As of December 31, 2017					
	Less than 12 months		12 Months or greater		Total	
			(in thousands)			
	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses
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)
Commercial paper	2,983	(3)	—	—	2,983	(3)
Total	$282,159	$ (534)	$ 62,745	$ (249)	$344,904	$ (783)

	As of December 31, 2016					
	Less than 12 months		12 Months or greater		Total	
			(in thousands)			
	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses
Corporate debt securities	$341,823	$ (510)	$178,818	$ (933)	$520,641	$ (1,443)
U.S. government and agency securities	19,479	(30)	6,699	(46)	26,178	(76)
Commercial paper	66,114	(71)	—	—	66,114	(71)
Total	$427,416	$ (611)	$185,517	$ (979)	$612,933	$ (1,590)

6. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following:

	December 31,	
	2017	2016
	(in thousands)	
Prepaid expenses and other receivables	$ 14,818	$ 6,145
Interest receivable	2,071	3,209
Prepaid expenses and other current assets	$ 16,889	$ 9,354

7. 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,	
		2017	2016
		(in thousands)	
Office equipment and software	3	$ 5,048	$ 4,942
Leasehold improvements	Over life of lease	14,665	6,668
Furniture and fixtures	7	5,257	4,202
Subtotal		24,970	15,812
Less: accumulated depreciation		(8,786)	(4,517)
Fixed assets, net		$ 16,184	$ 11,295

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

7. Fixed Assets, Net – (continued)

Depreciation expense for the years ended December 31, 2017, 2016 and 2015 was approximately $4.6 million, $3.8 million, and $1.7 million, respectively.

8. Inventory

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

	December 31,	
	2017	2016
	(in thousands)	
Work-in-process	$ 3,249	$ 2,207
Finished goods	231	72
Inventory, net	$ 3,480	$ 2,279

9. Accounts Payable, Accrued Expenses and Other Liabilities

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

	December 31,	
	2017	2016
	(in thousands)	
Accounts payable	$ 6,965	$ 6,722
Accrued employee compensation	27,118	19,287
Accrued contracted services and other	60,694	39,542
Accounts payable, accrued expenses and other liabilities	$ 94,777	$ 65,551

10. Long-Term Debt

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

	December 31,	
	2017	2016
	(in thousands)	
Long-term debt	$355,677	$ 341,356
Less current portion	—	—
Long-term debt outstanding	$355,677	$ 341,356

On July 6, 2016, the Company issued $460.0 million aggregate principal amount of the Convertible Notes. The Company received net proceeds 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 the net proceeds from the offering to fund the payment of 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 the Company. Interest is payable semi-annually on January 1 and July 1 of each year, beginning on January 1, 2017. The Convertible Notes mature on July 1, 2023, unless earlier repurchased, redeemed or converted. The Convertible Notes are convertible at the option of holders, under certain circumstances and during certain periods, into cash, shares of the Company's common stock 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. The Company may redeem for cash all or part of the Convertible Notes, at its option, on or after July 6, 2021, under certain circumstances at a redemption price

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

10. Long-Term Debt – (continued)

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 capped call transactions are expected generally to reduce the potential dilution 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 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 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 upon conversion of the Convertible Notes to the extent that such market price exceeds the cap price of the capped call transactions.

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 $29.3 million and $14.2 million for the year ended December 31, 2017 and 2016, respectively, related to the Convertible Notes. Accrued interest on the Convertible Notes was approximately $14.9 million and $7.3 million as of December 31, 2017 and 2016. The Company recorded debt issuance costs of $12.4 million, which are being amortized using the effective interest method. As of December 31, 2017 and 2016, $10.3 million and $11.7 million, respectively, of debt issuance costs are recorded on the consolidated balance sheet in Long-Term Debt, in accordance with ASU 2015-03. As of December 31, 2017 and 2016, the Company had outstanding borrowings of $460.0 million, related to the Convertible Notes.

11. Product Revenues, Net

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

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

	Years Ended December 31,	
	2017	2016
Product revenue, net:		
U.S.	$ 115.8	$ 18.2
ex-U.S.	13.4	—
Total product revenue, net	$ 129.2	$ 18.2

12. 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).

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

12. Fair Value Measurements – (continued)

- 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 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, 2017				
Assets:				
Money market funds	$ 13,361	$ 13,361	$ —	$ —
Available for sale 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	$ —
December 31, 2016				
Assets:				
Money market funds	$ 11,755	$ 11,755	$ —	$ —
Available for sale securities:				
Commercial paper	66,114	—	66,114	—
Corporate debt securities	553,418	—	553,418	—
U.S. government and agency securities	26,178	—	26,178	—
Total financial assets:	$ 657,465	$ 11,755	$ 645,710	$ —

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

12. Fair Value Measurements – (continued)

The estimated fair value of marketable debt securities (commercial paper, corporate debt securities, U.S. government and agency securities, and municipal securities) as of December 31, 2017 and 2016, respectively, by contractual maturity, are as follows:

	Fair Value as of December 31,	
	2017	2016
	(in thousands)	
Due in one year or less	$ 282,159	$ 456,184
Due after one year through 2 years	62,745	189,526
Total investments in debt securities	$ 344,904	$ 645,710

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

13. Stockholders' Equity and Preferred Stock

Common Stock

As of December 31, 2017 and 2016, the Company had 45,000,000 authorized shares of common stock, $0.001 par value per share, respectively. At the 2016 annual meeting of stockholders held on July 19, 2016, the Company's stockholders approved an amendment to the Company's restated certificate of incorporation, as amended, to increase the number of authorized shares of common stock from 35,000,000 shares to 45,000,000 shares.

In February 2015, the Company completed a public offering of 1,150,000 shares of its common stock at a public offering price of $176.00 per share. The shares were registered pursuant to a registration statement on Form S-3. After underwriting discounts and commissions and offering expenses, the Company received net proceeds of approximately $191.7 million.

In April 2015, the Company completed a public offering of 1,330,865 shares of its common stock pursuant to a registration statement on Form S-3. After underwriting discounts and commissions and offering expenses, the Company received net proceeds of approximately $367.1 million.

Dividends

The holders of common stock are entitled to receive dividends from time to time as declared by the board of directors. The Company has not declared 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

The holders of shares of common stock are entitled to one vote for each share held with respect to all matters voted on by the stockholders of the Company.

Preferred Stock

As of December 31, 2017 and 2016, the Company had 5,000,000 authorized shares of preferred stock, $0.001 par value per share, of which none are issued.

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

14. Stock Compensation

The 2012 Equity Incentive Plan (2012 Plan) became effective upon the pricing of the IPO in October 2012. At the same time, the 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 and 2012 Plans is 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 is determined utilizing the closing stock price on the date of grant. There were approximately 1.9 million and 1.5 million shares available for grant remaining under the 2012 Plan at December 31, 2017 and 2016, respectively. On January 1, 2017 and 2016, the numbers of shares reserved for issuance under the 2012 Plan was increased by 993,558, and 976,101 shares, respectively, as a result of the automatic increase in shares reserved pursuant to the terms thereof.

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,		
	2017	2016	2015
Volatility	61 – 65%	60 – 66%	61 – 90%
Expected term (in years)	6.0 – 9.9	5.1 – 10.0	5.1 – 7.0
Risk-free rate	1.8 – 2.4%	1.1 – 2.4%	0.2 – 2.2%
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 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 life at the grant date. The Company uses historical data to estimate the expected term of the option; separate groups of employees that have similar historical exercise behavior are considered separately for valuation purposes. The expected term of options granted represents the period of time the options are expected to be outstanding. The expected volatility was estimated based on historical volatility information of peer companies that are publicly available.

The Company's combined outstanding employee and non-employee option activity for the period from December 31, 2016 through December 31, 2017 is summarized as follows:

	Number of Shares (in thousands)	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2016	1,553	$ 117.80	7.4	$ 48,308
Granted	568	$ 107.00	—	$ —
Exercised	(109)	$ 26.01	—	$ —
Cancelled/forfeited	(133)	$ 137.66	—	$ —
Expired	(71)	$ 214.53	—	$ —
Outstanding at December 31, 2017	1,808	$ 114.70	7.4	$ 14,648
Expected to vest	1,808	$ 114.70	7.4	$ 14,648
Exercisable	923	$ 104.52	5.8	$ 14,648

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 shares that had exercise prices lower than the deemed fair value of the Company's common stock. As of December 31, 2017, the total compensation cost related to non-vested option awards not yet recognized is approximately

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

14. Stock Compensation – (continued)

$46.4 million with a weighted average remaining vesting period of 2.47 years. The weighted-average grant date fair value of options granted during the year ended December 31, 2017 is $63.65. The total fair value of shares underlying options that vested in 2017 was $26.6 million.

In April 2014, the Company issued 57,063 performance-based options to certain employees to purchase common stock 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 noted above. As of both December 31, 2017 and 2016, the achievement of the 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

The following table summarizes the aggregate activities in relation to RSU and RSA activity for the year ended December 31, 2017:

	Number of Shares (in thousands)	Weighted Average Grant Date Fair Value
Non-vested shares at December 31, 2016	381	$ 136.89
Granted	337	$ 102.35
Exercised	(155)	$ 137.26
Cancelled/forfeited	(70)	$ 133.77
Non-vested shares at December 31, 2017	493	$ 113.60

As of December 31, 2017, there was $42.5 million of unrecognized compensation expense related to unvested RSUs and RSAs, which is expected to be recognized over a weighted average of 2.51 years.

In October 2016, the Company issued 11,725 shares of restricted stock awards to a certain employee that will vest upon the achievement of certain regulatory and commercial milestones. For the year ended December 31, 2017, no stock-based compensation expense was recognized for these awards.

Stock-based compensation expense has been reported in our statements of operations as follows:

	Years Ended December 31,		
	2017	2016	2015
		(In thousands)	
Selling, general and administrative	$ 40,004	$ 32,073	$ 16,223
Research and development	16,964	14,132	17,966
Total stock-based compensation	$ 56,968	$ 46,205	$ 34,189

The Company accounts for forfeitures when they occur. Ultimately, the actual expense recognized over the vesting period will be for only those shares that vest. When performance based grants are issued, the Company recognizes no expense until achievement of the performance requirement is deemed probable.

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

15. Income Taxes

The components of loss before income taxes for the years ended December 31, 2017, 2016 and 2015 includes the following:

	Years Ended December 31,		
	2017	2016	2015
		(in thousands)	
United States	$(102,586)	$(154,812)	$ (116,349)
Foreign	(257,781)	(258,018)	(110,080)
Total	$(360,367)	$(412,830)	$ (226,429)

Income tax expense (benefit) differed from the amounts computed by applying the U.S. Federal income tax rate of 34% to loss before income taxes as a result of the following:

	Years Ended December 31,		
	2017	2016	2015
		(in thousands)	
Computed "expected" tax benefit	$(122,525)	$(140,362)	$ (76,986)
State taxes, net of U.S. Federal benefit	—	—	—
U.S. Federal rate reduction	84,787	—	—
U.S. Federal valuation allowance	282	40,377	40,973
Stock-based compensation	(49,391)	5,161	(3,230)
Officer compensation	26	50	(1,778)
Foreign tax rate differences	87,646	94,901	37,427
Intercompany license of intellectual property	—	—	3,400
Other	(825)	(127)	194
Total	$ —	$ —	$ —

The tax effects of temporary differences that give rise to the deferred tax assets and liabilities at December 31, 2017 and 2016 are presented below:

	December 31,	
	2017	2016
	(in thousands)	
Deferred tax assets:		
Net operating loss and other carryforwards	$ 276,481	$ 220,175
Stock compensation	14,651	17,166
Deferred revenue	1,149	2,400
Accrued compensation	3,994	4,775
Accrued expense	1,139	1,841
Intellectual property	1,059	3,570
Other	492	759
Deferred tax assets before valuation allowance	298,965	250,686
Valuation allowance	(282,730)	(223,383)
Total deferred tax assets	16,235	27,303
Deferred tax liabilities:		
Convertible Note	(16,235)	(27,303)
Total deferred tax liabilities	(16,235)	(27,303)
Net deferred tax asset (liability)	$ —	$ —

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

15. Income Taxes – (continued)

Effects of the Tax Cuts and Jobs Act

On December 22, 2017, the United States enacted tax reform legislation through the Tax Cuts and Jobs Act, which significantly changes the existing U.S. tax laws, including a reduction in the corporate tax rate to 21% effective for tax years including or commencing January 1, 2018 and a move from a worldwide tax system to a territorial system, limitations on the deductibility of interest expense and executive compensation, as well as other changes.

Given the significance of the legislation, the SEC staff issued Staff Accounting Bulletin No. 118 (SAB 118), which allows registrants to record provisional amounts during a one year "measurement period" similar to that used when accounting for business combinations. However, the measurement period is deemed to have ended earlier when the registrant has obtained, prepared and analyzed the information necessary to finalize its accounting. During the measurement period, impacts of the law are expected to be recorded at the time a reasonable estimate for all or a portion of the effects can be made, and provisional amounts can be recognized and adjusted as information becomes available, prepared or analyzed.

The SAB summarizes a three-step process to be applied at each reporting period to account for and qualitatively disclose: (1) the effects of the change in tax law for which accounting is complete; (2) provisional amounts (or adjustments to provisional amounts) for the effects of the tax law where accounting is not complete, but that a reasonable estimate has been determined; and (3) a reasonable estimate cannot yet be made and therefore taxes are reflected in accordance with law prior to the enactment of the Tax Cuts and Jobs Act.

Amounts recorded where accounting is complete principally relate 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.

The new law includes a one-time mandatory repatriation transition tax on the net accumulated earnings and profits of a U.S. taxpayer's foreign subsidiaries. The Company has performed an earnings and profits analysis, and as a result of accumulated losses since inception, there will be no income tax effect in the current or any future period. Therefore, the accounting for this matter is complete.

Effects of tax law changes where a reasonable estimate of the accounting effects has not yet been made include the excessive executive compensation limitation which could impact the deferred tax asset and associated valuation allowance related to stock compensation.

Other significant provisions that are not yet effective but may impact income taxes in future years include: an exemption from U.S. tax on dividends of future foreign earnings, limitation on the current deductibility of net interest expense in excess of 30 percent of adjusted taxable income, a limitation of net operating losses generated after January 1, 2018 to 80 percent of taxable income, an incremental tax (base erosion anti-abuse tax or BEAT) on excessive amounts paid to foreign related parties, and a minimum tax on certain foreign earnings in excess of 10 percent of the foreign subsidiaries tangible assets (i.e., global intangible low-taxed income or GILTI).

Effects of other Recent Accounting Pronouncements

In March 2016, the FASB issued ASU 2016-09, Improvements to Employee Share-Based Payment Accounting which is intended to improve the accounting for share-based payment transactions as part of the FASB's simplification initiative. The Company adopted ASU 2016-09 during the first quarter of 2017. As a result of this guidance, the Company recorded $58.7 million of additional deferred tax assets, which are fully offset by a valuation allowance.

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

15. Income Taxes – (continued)

Net Operating Losses

As of December 31, 2017 and 2016, the Company had net operating loss carryforwards, or NOLs, for U.S. Federal income tax purposes of $628.0 million and $562.3 million, respectively, which expire 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.

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 have 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. Additionally, tax laws limit the time during which NOLs and certain other tax attributes may be utilized against future taxes. 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, 2017 and 2016, 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 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, 2017 and 2016, the Company had no reserves for unrecognized tax benefits.

The Company and its subsidiaries are subject to taxation in the U.S. and various foreign jurisdictions. Of the major jurisdictions, the Company is subject to examination in: the United States for U.S. Federal purposes for 2014 and forward and generally for state purposes for 2013 and forward; and the United Kingdom for 2015 and forward. However, NOLs are subject to audit in any tax year in which those losses are utilized, notwithstanding the year of origin.

16. Commitments

Facility Leases

In May 2014, the Company entered into a lease agreement with The Irvine Company LLC for approximately 47,000 square feet in San Diego for office space. The lease term commenced in September 2014 and is scheduled to end in September 2019; however, the Company has an option to further extend the lease for an additional five-year term at market rates prevailing at such time. The rent for the first year was approximately $875,000 without giving effect to rent abatements and the rent will gradually increase every 12 months during the lease term. During the first nine months, the Company received a partial rent abatement from the landlord. The landlord provided the Company with an allowance of approximately $2.4 million for improvements to the office space.

In January 2016, Intercept Pharma Europe Ltd. (IPEL), a wholly owned subsidiary of the Company, entered into an underlease with Performing Right Society, Ltd., for office space in the King's Cross area of London, United Kingdom. The Company is the guarantor to the underlease. The underlease provided IPEL with 8,549 square feet of space. The lease term is anticipated to end on May 31, 2024. The annual rent is

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

16. Commitments – (continued)

approximately £726,665 (or approximately $1.0 million), payable quarterly. IPEL is also required to pay VAT on the rent. IPEL is responsible for a portion of the insurance, certain service charges and taxes for the building based on the floor area rented by them.

In February 2016, the Company entered into a sublease with Restoration Hardware, Inc. for additional office space in New York City. The sublease provided the Company with an additional 10,785 square feet of space. The lease term is anticipated to end in July 2021. The annual rent is approximately $1.0 million payable monthly. The Company is also responsible for its proportionate share of increases in operating expenses beginning January 2017 as well as its proportionate share of increases in real estate taxes over the average of the 2015/2016 and 2016/2017 fiscal years.

In December 2016, the Company entered into a lease agreement relating to the Company's new global corporate headquarters in the Hudson Yards development site in New York, New York. The lease provided the Company with office space in 10 Hudson Yards (the "10 Building") where we lease and occupy an aggregate of approximately 45,500 square feet of office space. The lease for our current corporate headquarters will expire in July 2021.

In December 2017, we terminated the lease agreement relating to 55 Hudson Yards and have chosen to stay in our current 10 Hudson Yards location in order to reduce our long-term lease obligations. We incurred $9.8 million in expenses, which included a $7.8 million termination fee. In addition, we also reduced our future operating lease obligation by $124.5 million over the life of that lease.

Rent expense under operating leases for facilities for the years ended December 31, 2017, 2016 and 2015 was approximately $8.9 million, $5.5 million, and $3.8 million, respectively. As of December 31, 2017, minimum operating lease payments under non-cancelable leases, as amended, are as follows:

Year Ending December 31,	Amount
	(in thousands)
2018	$ 7,602
2019	6,595
2020	5,720
2021	3,894
2022	2,631
Thereafter	3,935
Total future minimum operating lease payments	$ 30,377

Purchase Commitments

The Company enters into license and research and development agreements with universities and other third parties. The Company enters into contracts in the normal course of business with contract research organizations for clinical trials, clinical and commercial supply manufacturing, with vendors for preclinical research studies and for other services and products for operating purposes. The agreements generally provide for termination within 90 days of notice. Such agreements are cancelable contracts and not included as purchase commitments. The Company has included as purchase obligations the Company's commitments under agreements to the extent they are quantifiable and are not cancelable, which is approximately $40.2 million as of December 31, 2017.

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

17. Net Loss Per Share

The following table presents the historical computation of basic and diluted net loss per share:

	Years Ended December 31,		
	2017	2016	2015
	(in thousands, except per share amounts)		
Historical Net loss per share			
Numerator:			
Net loss attributable to common stockholders	$(360,367)	$(412,830)	$ (226,429)
Denominator:			
Weighted average shares outstanding, basic and diluted	25,054	24,663	23,694
Net loss per share, basic and diluted	$ (14.38)	$ (16.74)	$ (9.56)

The following potentially dilutive securities have been excluded from the computations of diluted weighted average shares outstanding as of December 31, 2017, 2016 and 2015, as they would have been anti-dilutive:

	December 31,		
	2017	2016	2015
		(in thousands)	
Options	1,808	1,553	1,348
Restricted stock units	493	382	193
Total	2,301	1,935	1,541

18. Quarterly Financial Data (unaudited)

The following table summarizes the unaudited quarterly financial data for the years ended December 31, 2017 and 2016;

	Quarters Ended				
	March 31,	June 30,	September 30,	December 31,	Total
	(in thousands, except for per share amounts)				
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)	
2016					
Revenues	$ 445	$ 5,520	$ 5,177	$ 13,809	$ 24,951
Operating loss	(127,400)	(78,095)	(83,036)	(114,007)	(402,538)
Net loss	(126,674)	(77,299)	(88,815)	(120,042)	(412,830)
Net loss per common share – basic and diluted	$ (5.17)	$ (3.14)	$ (3.59)	$ (4.84)	

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

19. Litigation

On February 21, 2014 and February 28, 2014, purported shareholder class actions, styled *Scot H. Atwood v. Intercept Pharmaceuticals, Inc. et al.* and *George Burton v. Intercept Pharmaceuticals, Inc. et al.*, respectively, 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 claim 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 Securities Exchange Act of 1934, as amended, and Rule 10b-5 promulgated thereunder. The alleged improper disclosures relate 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.

On April 22, 2014, two individuals each moved to consolidate the cases and a lead plaintiff was subsequently appointed by the Court. On June 27, 2014, the lead plaintiff filed an amended complaint on behalf of the putative class as contemplated by the order of the Court. The lead plaintiff was seeking unspecified monetary damages on behalf of the putative class and an award of costs and expenses, including attorneys' fees. On August 14, 2014, the defendants filed a motion to dismiss the complaint. Oral arguments on the motion to dismiss were held on February 24, 2015. On March 4, 2015, the defendants' motion to dismiss was denied by the Court. The defendants answered the amended complaint on April 13, 2015. On July 15, 2015, the plaintiff moved for class certification and appointment of class representatives and class counsel. On September 14, 2015, the defendants opposed the plaintiff's class certification motion. The plaintiff filed its reply to the defendants' opposition on October 14, 2015, to which the defendants filed a sur-reply on November 10, 2015. Oral arguments on the class certification motion were held on January 20, 2016.

On May 2, 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 on May 5, 2016. On May 23, 2016, 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 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. On September 8, 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 do not admit any liability as part of the settlement.

20. Restructuring Charges

In December 2017, the Company initiated a 15% reduction in the workforce and the affected employees were subsequently notified. 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 is expected to be paid out in the first quarter of 2018.

INTERCEPT PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

21. Subsequent Events

On February 13, 2018, the Company entered into an amendment to its exclusive license agreement with Sumitomo Dainippon. Under the new terms of the license agreement, Sumitomo Dainippon agreed to return the rights to develop and commercialize OCA in Japan and Korea and the Company agreed to forego any further milestone or royalty payments relating to the development and commercialization of OCA in such countries. In addition, Sumitomo Dainippon waived its option rights to develop OCA in any country outside of China and the parties adjusted certain milestone payment obligations with respect to the development and commercialization of OCA. The parties also agreed that if certain clinical development milestones in China are not met by December 31, 2020, Sumitomo Dainippon may choose either to pay the Company a milestone payment or terminate the Agreement.

TABLE OF CONTENTS

Exhibit List

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
3.1	Restated Certificate of Incorporation, as amended	_	Form 10-Q (Exhibit 3.1)	08/09/16	001-35668
3.2	Restated Bylaws of the Registrant	_	Form 8-K (Exhibit 3.2)	02/17/16	001-35668
4.1	Form of Common Stock Certificate of the Registrant	_	Form S-8 (Exhibit 4.3)	11/07/12	333-184810
4.2	Third Amended and Restated Stockholders Agreement by and among the Registrant, the holders of the Registrant's convertible preferred stock, the Registrant's founders and certain other investors, dated August 9, 2012	_	Form S-1 (Exhibit 4.2)	09/04/12	333-183706
4.3	Indenture by and between the Registrant and U.S. Bank National Association, a national banking association, as trusted, dated July 6, 2016	_	Form 8-K (Exhibit 4.1)	07/06/16	001-35668
4.4	First Supplemental Indenture (including the Form of Note) by and between the Registrant and U.S. Bank National Association, a national banking association, as trustee, dated July 6, 2016	_	Form 8-K (Exhibit 4.2)	07/06/16	001-35668
4.5	Form of Senior Indenture	_	Form S-3 (Exhibit 4.1)	5/10/17	333-217861
4.6	Form of Subordinated Indenture	_	Form S-3 (Exhibit 4.2)	5/10/17	333-217861
4.7	Form of Senior Note	_	Form S-3 (Exhibit 4.3)	5/10/17	333-217861
4.8	Form of Subordinated Note	_	Form S-3 (Exhibit 4.4)	5/10/17	333-217861
10.1.1	Call Option Confirmation by and between the Registrant and Royal Bank of Canada, dated June 30, 2016	_	Form 8-K (Exhibit 10.1)	07/06/16	001-35668
10.1.2	Additional Call Option Confirmation by and between the Registrant and Royal Bank of Canada, dated July 1, 2016	_	Form 8-K (Exhibit 10.2)	07/06/16	001-35668
10.1.3	Call Option Confirmation by and between the Registrant and UBS AG, London Branch, dated June 30, 2016	_	Form 8-K (Exhibit 10.3)	07/06/16	001-35668

TABLE OF CONTENTS

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
10.1.4	Additional Call Option Confirmation by and between the Registrant and UBS AG, London Branch, dated July 1, 2016	_	Form 8-K (Exhibit 10.4)	07/06/16	001-35668
10.1.5	Call Option by and between the Registrant and Credit Suisse Capital LLC, dated June 30, 2016	_	Form 8-K (Exhibit 10.5)	07/06/16	001-35668
10.1.6	Additional Call Option by and between the Registrant and Credit Suisse Capital LLC, dated July 1, 2016	_	Form 8-K (Exhibit 10.6)	07/06/16	001-35668
10.2	Commercial Manufacturing and Supply Agreement by and between the Registrant and PharmaZell GMBH, dated August 12, 2016*	_	Form 10-Q (Exhibit 10.8)	11/09/16	001-35668
10.2.1	Amendment #1 to Manufacturing and Supply Agreement by and between the Registrant and PharmaZell GMBH, dated December 12, 2017*	X	_	_	_
Equity Compensation Plans					
10.3.1	Form of 2012 Equity Incentive Plan of the Registrant+	_	Amendment No. 1 to Form S-1 (Exhibit 10.2.1)	09/27/12	333-183706
10.3.2	Form of Stock Option Grant Notice for Directors under the 2012 Equity Incentive Plan of the Registrant+	_	Amendment No. 1 to Form S-1 (Exhibit 10.2.2)	09/27/12	333-183706
10.3.3	Form of Stock Option Grant Notice for Employees and Consult ants under the 2012 Equity Incentive Plan of the Registrant+	_	Amendment No. 1 to Form S-1 (Exhibit 10.2.3)	09/27/12	333-183706
10.3.4	Form of Restricted Stock Unit Award Grant Notice for Directors under the 2012 Equity Incentive Plan of the Registrant+	_	Amendment No. 1 to Form S-1 (Exhibit 10.2.4)	09/27/12	333-183706
10.3.5	Form of Restricted Stock Unit Award Grant Notice for Employees and Consultants under the 2012 Equity Incentive Plan of the Registrant+	_	Amendment No. 1 to Form S-1 (Exhibit 10.2.5)	09/27/12	333-183706
10.3.6	Form of Restricted Stock Award Grant Notice for Directors under the 2012 Equity Incentive Plan of the Registrant+	_	Form 10-Q (Exhibit 10.3)	05/09/14	001-35668

TABLE OF CONTENTS

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
10.3.7	Form of Restricted Stock Award Grant Notice for Employees and Consultants under the 2012 Equity Incentive Plan of the Registrant+	_	Form 10-Q (Exhibit 10.4)	05/09/14	001-35668
10.4	Non-Employee Director Compensation Policy+	_	Form 8-K (Exhibit 10.1)	02/17/16	001-35668
Agreements with Executive Officers and Directors					
10.5	Amended and Restated Employment Agreement by and between the Registrant and Mark Pruzanski, dated May 14, 2013+	_	Form 10-Q (Exhibit 10.5)	05/14/13	001-35668
10.6	Amended and Restated Employment Agreement by and between the Registrant and David Shapiro, effective as of November 27, 2017+	_	Form 8-K (Exhibit 10.2)	12/01/17	001-35668
10.7	Employment Agreement by and between the Registrant and Rachel McMinn, effective as of April 30, 2014+	_	Form 10-Q (Exhibit 10.2)	05/09/14	001-35668
10.8	Separation Agreement by and between the Registrant and Rachel McMinn, effective as of December 31, 2017+	X	_	_	_
10.9	Employment Agreement by and between the Registrant and Sandip S. Kapadia, effective as of May 3, 2016+	_	Form 10-Q (Exhibit 10.1.1)	08/09/16	001-35668
10.10	Employment Agreement by and between the Registrant and Lisa Bright, effective as of October 7, 2016+	_	Form 10-K (Exhibit 10.11)	03/01/17	001-35668
10.11	Employment Agreement by and between the Registrant and Jerome B. Durso, effective as of February 15, 2017+	_	Form 10-Q (Exhibit 10.1)	05/10/17	001-35668
10.12	Employment Agreement by and between the Registrant and David Ford, effective as of April 14, 2017+	_	Form 10-Q (Exhibit 10.1)	08/03/17	001-35668
10.13	Employment Agreement by and between the Registrant and Christian Weyer, effective as of November 27, 2017+	_	Form 8-K (Exhibit 10.1)	12/01/17	001-35668
10.14	Form of Indemnification Agreement by and between the Registrant and each of its directors and executive officers	_	Form S-1 (Exhibit 10.7)	09/04/12	333-183706

TABLE OF CONTENTS

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
Lease Agreements					
10.15	Lease Agreement between Jamestown 405 West 15th Street, L.P. and the Registrant, dated October 15, 2013	_	Form 8-K (Exhibit 10.1)	10/21/13	001-35668
10.16.1	Lease Agreement between The Irvine Company LLC and the Registrant, dated May 1, 2014	_	Form 8-K (Exhibit 10.1)	05/07/14	001-35668
10.16.2	Amended Lease Agreement between the Irvine Company LLC and the Registrant, dated July 19, 2016	_	Form 10-Q (Exhibit 10.7)	11/09/16	001-35668
10.17	Underlease between the Registrant and Merck Sharp & Dohme Limited, dated February 19, 2015	_	Form 8-K (Exhibit 10.1)	02/24/15	001-35668
10.18	Underlease between the Registrant, Intercept Pharma Europe, Ltd. and Performing Right Society, Ltd., dated January 22, 2016	_	Form 10-K (Exhibit 10.12)	02/29/16	001-35668
10.19	Office Sublease between the Registrant and Restoration Hardware, Inc., dated February 23, 2016	_	Form 10-K (Exhibit 10.13)	02/29/16	001-35668
10.20	First Amendment to Lease Agreement between Legacy Yards Tenant LP and the Registrant, dated June 27, 2017	_	Form 10-Q (Exhibit 10.1)	11/06/17	001-35668
10.21	Termination of Lease between Hudson Yards Owner LLC and the Registrant, dated December 31, 2017	X	_	_	_
Agreements with Respect to Collaborations, Licenses, Research and Development					
10.22	License Agreement by and between the Registrant and Sumitomo Dainippon Pharma Co. Ltd., dated March 29, 2011*	_	Amendment No. 1 to Form S-1 (Exhibit 10.10)	09/27/12	333-183706
Other Exhibits					
12.1	Computation of Ratio of Earnings to Fixed Charges for the Year Ended December 31, 2016	X	_	_	_
21.1	Subsidiaries of the Registrant	X	_	_	_
23.1	Consent of KPMG LLP, independent registered public accounting firm	X	_	_	_
31.1	Certification of the Chief Executive Officer	X	_	_	_
31.2	Certification of the Chief Financial Officer	X	_	_	

TABLE OF CONTENTS

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
32	Certification pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	X	_	_	_
101	The following materials from Intercept Pharmaceuticals, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2017, formatted in XBRL (eXtensible Business Reporting Language): (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations and Comprehensive Loss, (iii) Consolidated Statements of Changes in Stockholders' Equity, (iv) Consolidated Statements of Cash Flows, and (v) Notes to Consolidated Financial Statements	X			

(+) Management contract or compensatory plan or arrangement.

(*) Portions of this exhibit have been omitted pursuant to a request for confidential treatment.

Exhibit 10.2.1

Execution Version

Confidential Materials omitted and filed separately with the
Securities and Exchange Commission. Double asterisks denote omissions.

AMENDMENT #1 TO
MANUFACTURING AND SUPPLY AGREEMENT

THIS AMENDMENT #1 TO MANUFACTURING AND SUPPLY AGREEMENT (this "**Amendment #1**") dated the 12th day of December, 2017 (the "**Amendment #1 Effective Date**") is made by and between Intercept Pharma Europe Ltd., having a location at 2 Pancras Square, Floor 1, London, United Kingdom N1C 4AG ("**Intercept**"), and PharmaZell GmbH, a corporation organized under the laws of Germany ("**PharmaZell**"). Intercept and PharmaZell are sometimes referred to herein individually as a "**Party**" and collectively as the "**Parties**."

WHEREAS, Intercept and PharmaZell previously entered into that certain Manufacturing and Supply Agreement dated August 12, 2016 (the "**Agreement**");

WHEREAS, the Parties desire to amend the Agreement on the terms and conditions set forth in this Amendment #1.

NOW, THEREFORE, in consideration of the foregoing premises, the mutual promises and covenants of the Parties contained herein, and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties, intending to be legally bound, do hereby agree as follows:

1. Capitalized terms used but not defined in this Amendment #1 shall have the meanings ascribed thereto in the Agreement.

2. With respect to the [**] validation campaign of API under the proposal dated August 24, 2014 (the " **Existing Work Order**"), provided that PharmaZell has provided to Intercept on or before the Amendment #1 Effective Date the validation documentation for the Supplied Material and evidence that approximately [**] of the Supplied Material that is the subject of such Existing Work Order has been shipped to Intercept in accordance with the terms and conditions of the Agreement, Intercept shall pay to PharmaZell on or before [**] the amount of [**] as full and final payment for the Supplied Material that is the subject of such Existing Work Order.

3. Notwithstanding the ordering, delivery dates and payment provisions set forth in the Agreement or Work Order #1, with respect to the Supplied Material that is the subject of Work Order #1 ("**Campaign 1**"), such Work Order will be amended and replaced with the Work Orders attached to this Amendment #1 as Exhibit 1 and Exhibit 2 and the following shall apply:

3.1 The Parties agree that PharmaZell has achieved [**] Steps of the Manufacturing Process and has invoiced Intercept for the same. Intercept shall pay to PharmaZell on or before [**] the amount of [**] for the achievement of [**] Steps of the Manufacturing Process as invoiced by PharmaZell.

3.2 With respect to [**] Steps of the Manufacturing Process, in accordance with the Agreement, this Amendment #1 and the Work Order attached hereto as Exhibit 1, PharmaZell shall Manufacture and invoice the Supplied Material that is the subject of Campaign 1 based on a [**] Supplied Material order size at a price per [**] equal to [**] (even though the Work Order attached hereto as Exhibit 1 is for [**] (subject to the [**] cap of Section 2.7(f) of the Agreement (i.e., Intercept shall have no obligation to purchase more than [**] of Campaign 1))) in accordance with the terms and conditions of the Agreement with the expected dates as follows:

Milestone	Step of Manufacturing Process	Percentage of total Purchase Price	Required Date of Completion of Step of Manufacturing Process
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]

The required Delivery Date for [**] is set forth in the Work Order attached hereto as Exhibit 1.

3.3 Upon the completion of the [**] Step of the Manufacturing Process, PharmaZell shall divide the amount of [**] into [**], [**] of which shall be the "**Campaign 1 Processed Amount**" and [**] of which shall be the "**Campaign 1 Stored Amount**".

(a) PharmaZell, in accordance with the terms and conditions of the Agreement, this Amendment #1 and the Work Order attached hereto as Exhibit 2, shall process and Manufacture the Campaign 1 Processed Amount into API, and upon completion, shall provide the documentation and deliver to Intercept the API resulting from the Campaign 1 Processed Amount. PharmaZell shall invoice Intercept for the Campaign 1 Processed Amount in an amount equal to [**] of the total Purchase Price for Campaign 1 (based on [**]). The required Delivery Date for the API from the Campaign 1 Processed Amount is set forth in the Work Order attached hereto as Exhibit 2.

(b) With respect to the Campaign 1 Stored Amount, such Campaign 1 Stored Amount shall be considered "Intercept Material" and stored and handled by PharmaZell in accordance with the terms and conditions of Sections 2.7(a)-(d) of the Agreement and such additional storage and handling conditions as are set forth in the Quality Agreement and the Work Order attached hereto as Exhibit 2. On or before [**], Intercept shall notify PharmaZell that Intercept either desires PharmaZell to (a) Manufacture the Campaign 1 Stored Amount into API and deliver such API to Intercept in accordance with the terms and conditions of the Agreement or (b) continue to store the Campaign 1 Stored Amount as Intercept Material beyond [**].

(c) In the event that Intercept requires PharmaZell to Manufacture the Campaign 1 Stored Amount into API, Intercept shall issue a new Work Order by [**] for such Manufacturing and specify the requested Delivery Date therefor (it being understood that with respect to the Delivery Date for the API to be Manufactured from the Campaign 1 Stored Amount, Intercept shall have the right to specify a Delivery Date that is [**] months after the issuance of such Work Order). Upon the delivery of the API resulting from the Campaign 1 Stored Amount, PharmaZell shall invoice Intercept for the remaining percentage of the Purchase Price (at a price per [**] of [**]) in accordance with the Agreement based on the amount of API actually delivered (taking into account the total amount of API delivered from the Campaign 1 Processed Amount and the Campaign 1 Stored Amount).

(d) In the event that Intercept requires PharmaZell to continue to store the Campaign 1 Stored Amount, (i) PharmaZell shall continue to store such Campaign 1 Stored Amount until the earlier of (x) the expiration or termination of the Agreement or (y) such time as Intercept requires PharmaZell to Manufacture the Campaign 1 Stored Amount into API, and (ii) PharmaZell shall invoice Intercept for [**] of the Purchase Price based on an expected yield conversion of [**] from [**] to API, (subject to a cap of [**] of API). At any time during the Term, Intercept may issue a Work Order with a requested Delivery Date for PharmaZell to Manufacture the Campaign 1 Stored Amount into API (it being understood that with respect to the Delivery Date for the API to be Manufactured from the Campaign 1 Stored Amount, Intercept shall have the right to specify a Delivery Date that is [**] months after the issuance of such Work Order). Upon the delivery of the API resulting from the Campaign 1 Stored Amount, PharmaZell shall invoice Intercept for the remaining percentage of the Purchase Price in accordance with the Agreement based on the amount of API actually delivered (taking into account the amount of API delivered from the Campaign 1 Processed Amount and the Campaign 1 Stored Amount). If Intercept has not required PharmaZell to Manufacture the Campaign 1 Stored Amount into API prior to the expiration or termination of the Agreement, upon the written direction of Intercept, PharmaZell shall either deliver such Campaign 1 Stored Amount to Intercept or its designee or destroy such Campaign 1 Stored Amount.

4. On the Amendment Effective Date, Intercept is hereby issuing the Work Orders for [**] of API, with the Work Order attached as Exhibit 3 for the manufacture of such campaign through [**] and the Work Order attached hereto as Exhibit 4 for the manufacture of [**] into API. Notwithstanding the ordering, delivery dates and payment provisions set forth in the Agreement, with respect to the API that is the subject of the Work Orders attached hereto as Exhibit 3 and Exhibit 4 ("**Campaign 2**"), the following shall apply:

4.1 With respect to the [**] Steps of the Manufacturing Process, PharmaZell shall Manufacture and invoice the Supplied Material that is the subject of Campaign 2 based on a [**] Supplied Material order size (subject to the [**] cap of Section 2.7(f) of the Agreement (i.e., Intercept shall have no obligation to purchase more than [**] of Campaign 2) in accordance with the terms and conditions of the Agreement and the below table:

Milestone	Step of Manufacturing Process	Percentage of total Purchase Price	Required Date of Completion of Step of Manufacturing Process
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]

The required Delivery Date for the [**] from the Campaign 2 Processed Amount is set forth in the Work Order attached hereto as Exhibit 3.

4.2 Upon the completion of the [**] Step of the Manufacturing Process, PharmaZell shall divide the amount of [**] into [**], [**] of which shall be the "**Campaign 2 Processed Amount**" and [**] of which shall be the "**Campaign 2 Stored Amount**".

(a) PharmaZell, in accordance with the terms and conditions of the Agreement, this Amendment #1 and the Work Order attached hereto as Exhibit 4 shall process and Manufacture the Campaign 2 Processed Amount into API, and upon completion, shall provide the documentation and deliver to Intercept the API resulting from the Campaign 2 Processed Amount. PharmaZell shall invoice Intercept for the Campaign 2 Processed Amount in amount equal to [**] of the total Purchase Price for Campaign 2 (based on [**]). The required Delivery Date for the API from the Campaign 2 Processed Amount is set forth in the Work Order attached hereto as Exhibit 4.

(b) With respect to the Campaign 2 Stored Amount, such Campaign 2 Stored Amount shall be considered "Intercept Material" and shall be stored and handled by PharmaZell in accordance with the terms and conditions of Sections 2.7(a)-(d) of the Agreement and such additional storage and handling conditions as are set forth in the Quality Agreement and the Work Order attached hereto as Exhibit 4. On or before [**], Intercept shall notify PharmaZell that Intercept either desires PharmaZell to (a) Manufacture the Campaign 2 Stored Amount into API and deliver such API to Intercept in accordance with the terms and conditions of the Agreement or (b) continue to store the Campaign 2 Stored Amount as Intercept Material beyond [**]; provided that the [**] date shall be extended day-for-day for every day that PharmaZell delivers the [**] beyond the Delivery Date for such [**] set forth in the Work Order attached as Exhibit 3.

(c) In the event that Intercept requires PharmaZell to Manufacture the Campaign 2 Stored Amount into API, Intercept shall issue a new Work Order for such Manufacturing by the later of [**] or [**], and specify the requested Delivery Date therefor (it being understood that with respect to the Delivery Date for the API to be Manufactured from the Campaign 2 Stored Amount, Intercept shall have the right to specify a Delivery Date that is [**] months after the issuance of such Work Order). Upon the delivery of the API resulting from the Campaign 2 Stored Amount, PharmaZell shall invoice Intercept for the remaining percentage of the Purchase Price in accordance with the Agreement based on the amount of API actually delivered (taking into account the total amount of API delivered from the Campaign 2 Processed Amount and the Campaign 2 Stored Amount).

(d) In the event that Intercept requires PharmaZell to continue to store the Campaign 2 Stored Amount, (i) PharmaZell shall continue to store such Campaign 2 Stored Amount until the earlier of (x) the expiration or termination of the Agreement or (y) such time as Intercept requires PharmaZell to Manufacture the Campaign 2 Stored Amount into API, and (ii) PharmaZell shall invoice Intercept for [**]of the Purchase Price based on an expected yield conversion of [**] from [**] to API (subject to a cap of [**] of API). At any time during the Term, Intercept may issue a Work Order with a requested Delivery Date for PharmaZell to Manufacture the Campaign 2 Stored Amount into API (it being understood that with respect to the Delivery Date for the API to be Manufactured from the Campaign 2 Stored Amount, Intercept shall have the right to specify a Delivery Date that is [**] months after the issuance of such Work Order). Upon the delivery of the API resulting from the Campaign 2 Stored Amount, PharmaZell shall invoice Intercept for the remaining percentage of the Purchase Price in accordance with the Agreement based on the amount of API actually delivered (taking into account the amount of API delivered from the Campaign 2 Processed Amount and the Campaign 2 Stored Amount). If Intercept has not required PharmaZell to Manufacture the Campaign 2 Stored Amount into API prior to the expiration or termination of the Agreement, upon the written direction of Intercept, PharmaZell shall either deliver such Campaign 2 Stored Amount to Intercept or its designee or destroy such Campaign 2 Stored Amount.

5. The Parties acknowledge and agree that, notwithstanding anything to the contrary contained in Section 2.2(b) of the Agreement, the issuance of the Work Orders attached hereto for Campaign 1 has satisfied Intercept's Minimum Annual Requirement for Calendar Year 2017 and the issuance of the Work Orders attached hereto for Campaign 2 has satisfied Intercept's Minimum Annual Requirement for Calendar Year 2018, and Intercept shall have no further obligations to order any quantities of Supplied Material for delivery in either Calendar Year 2017 or Calendar Year 2018.

6. Schedule 2.2(b) of the Agreement is hereby deleted.

7. Schedule 2.7(e) of the Agreement is hereby replaced in its entirety with the Schedule 2.7(e) attached to this Amendment #1 as Appendix 1.

8. Except as specifically amended hereby, the Agreement remains in full force and effect.

9. The Governing Law and Dispute Resolution provisions contained in Sections 10.6 and 10.7 of the Agreement shall apply to any disputes under this Amendment #1 as if fully set forth herein.

10. This Amendment #1 may be executed in any number of counterparts, each of which shall be deemed to be an original, and all of which, taken together, shall constitute one and the same instrument. Delivery of an executed counterpart of a signature page of this Amendment #1 (and each amendment, modification and waiver in respect of it) by facsimile or other electronic transmission shall be as effective as delivery of a manually executed original counterpart of each such instrument.

11. This Amendment #1 shall be written and executed in, and all other communications under or in connection with this Amendment #1 shall be in, the English language. Any translation into any other language shall not be an official version thereof, and in the event of any conflict in interpretation between the English version and such translation, the English version shall control.

Signature Page to Follow

IN WITNESS WHEREOF, the Parties hereto have executed this Amendment #1 to be effective as of the last date of signature below.

INTERCEPT PHARMA EUROPE LTD.	PHARMAZELL GmbH
By: /s/ Daniel Hood	By: /s/ Dr. Wolfgang Burger
Name: Daniel Hood	Name: Dr. Wolfgang Burger
Title: Authorized Signatory	Title: VP Business Development
Date: December 12, 2017	Date: December 12, 2017

APPENDIX 1

Schedule 2.7(e)

Standard Yields

[**]

Exhibit 10.8

EXECUTION VERSION

SEPARATION AGREEMENT

This Separation Agreement (the "***Agreement***") is between Rachel McMinn ("***Employee***"), on behalf of Employee and all of Employee's heirs, executors, administrators and successors (individually and collectively, "***Releasors***") and Intercept Pharmaceuticals, Inc. (the "***Company***"), on behalf of the Company and all of its past, present, and future parents, subsidiaries, divisions, affiliates, directors, officers, managers, members, agents, successors, assigns, former employees and employees (individually and collectively, the "***Company Parties***") for the purpose of the termination of Employee's employment relationship with the Company effective December 31, 2017 (the "***Termination Date***") and detailing their respective rights and obligations.

1. Transition; Separation.

a. Effective on November 1, 2017 (the "Transition Date") Employee shall resign from her position as Chief Business and Strategy Officer. During the period beginning on the Transition Date and ending on the Termination Date (such period, the "Transition Period"), the Employee will continue to be employed by the Company as a Strategic Advisor to the Chief Executive Officer and perform such duties as the Company may request from time to time. During the Transition Period, the Company will continue to pay Employee her base salary at the rate in effect as of the date hereof and Employee will continue to participate in the Company's health and welfare plans, subject to their terms.

b. Effective on the Termination Date, Employee's employment relationship with the Company shall terminate in full. Employee acknowledges that from and after the Termination Date, Employee shall have no authority to, and shall not represent herself as an employee of the Company.

2. Consideration.

a. As consideration for Employee's execution of this Agreement and for the other promises set forth in this Agreement, and provided Employee executes and does not rescind her assent to this Agreement, and within sixty (60) days after the Termination Date Employee executes and does not rescind her assent to the Supplemental Release of Claims set forth in Exhibit A (the "Supplemental Release"), the Company shall pay or provide Employee with the following (the "Separation Benefits"):

i. twelve (12) months of Employee's base salary in effect as of the Termination Date, payable according to the Company's payroll commencing on the first payroll date following the date the Supplemental Release is effective and irrevocable (the "Payment Date");

ii. for a period of twelve (12) months following the Termination Date, continue Employee's participation in the Company's group health plan and dental plan and shall pay that portion of the premiums that the Company paid on behalf of Employee and her dependents during Employee's employment, provided, however, that if the Company's health insurance plan and/or dental plan does not permit such continued participation in such plan after Employee's termination of employment, then the Company shall pay that portion of the premiums associated with COBRA continuation coverage that the Company paid on behalf of Employee and her dependents during Employee's employment, including any administrative fee, on Employee's behalf for such twelve (12) month period; and provided, further, that if Employee becomes employed with another employer during the period in which continued health insurance and/or dental insurance is being provided pursuant to this Section, the Company shall not be required to continue such health and dental benefits, or if applicable, to pay the costs of COBRA, if Employee becomes covered under a health insurance plan of the new employer. For purposes of this Section 2.a.ii, the term "Employee" shall include, to the extent applicable, Employee's spouse and any of her dependents covered under the Company's group health plan and/or dental plan prior to her termination of employment;

iii. bonus for the 2017 calendar year equal to 40% of Employee's base salary; and

iv. the number of Employee's unvested stock options and other equity-based awards that would otherwise have vested from the Termination Date to the first anniversary of the Termination Date shall vest as of the date the Supplemental Release becomes effective and irrevocable and Employee (or her estate or legal representative, if applicable) shall have until the earlier of the expiration date of the option or one (1) year from the Termination Date to exercise all vested options unless the stock plan pursuant to which the option is granted requires earlier termination in connection with a liquidation or sale of the Company. For purposes of clarity, Employee's outstanding vested stock options and other equity as of immediately following the date the Supplemental Release becomes effective and irrevocable are set forth in Exhibit B

v. a bonus of $5,000, payable on the Payment Date, such amount intended to go towards the payment of Employee's legal fees incurred in connection with the negotiation of this Agreement.

b. Employee acknowledges and agrees that Employee will only be entitled to the consideration under Sections 2.a if Employee signs this Agreement and the Supplemental Release becomes effective and irrevocable; and Employee further acknowledges and understands that the compensation and benefits set forth in Section 5.1 of the Employment Agreement between Employee and the Company, dated April 30, 2014 (the "Employment Agreement") shall be paid or provided to Employee regardless of whether Employee executes this Agreement. The consideration described in Section 2.a are in complete satisfaction of any and all claims described in the Supplemental Release and the Employment Agreement.

c. In the event that Employee's employment with the Company is terminated for any reason prior to the Termination Date, then the Termination Date shall be the date of such termination.

3. Release of Claims. FOR AND IN CONSIDERATION OF the Separation Benefits, which Separation Benefits are conditioned on Employee signing this release of claims ("Release") and the Supplemental Release, which Employee will forfeit unless Employee executes and does not revoke this Agreement, Employee, on her own behalf and on behalf of her heirs and estate, voluntarily, knowingly and willingly release and forever discharge the Company, its subsidiaries, affiliates, parents, and, in their capacities as such, stockholders, together with each of those entities' respective officers, directors, stockholders, employees, agents, fiduciaries and administrators, each in their capacities as such (collectively, the "Releasees") from any and all claims and rights of any nature whatsoever which Employee now has or in the future may have against them up to the date Employee executes this Agreement, whether known or unknown, suspected or unsuspected. This Release includes, but is not limited to, any rights or claims relating in any way to my employment relationship with the Company or any of the other Releasees or the termination thereof, any contract claims (express or implied, written or oral), including, but not limited to, the Employment Agreement, or any rights or claims under any statute, including, without limitation, the Americans with Disabilities Act, the Age Discrimination in Employment Act, the Older Workers' Benefit Protection Act, the Rehabilitation Act of 1973 (including Section 504 thereof), Title VII of the 1964 Civil Rights Act, the Civil Rights Act of 1866 (42 U.S.C. § 1981), the Civil Rights Act of 1991, the Equal Pay Act, the National Labor Relations Act, the Worker Adjustment and Retraining Notification Act, the Family Medical Leave Act, the Lilly Ledbetter Fair Pay Act, the Genetic Information Non-Discrimination Act, the New York State Human Rights Law, the New York City Human Rights Law, and the Employee Retirement Income Security Act of 1974, all as amended, and any other federal, state or local law. This Release specifically includes, but is not limited to, any claims based upon the right to the payment of wages, incentive and performance compensation, bonuses, equity grants, vacation, pension benefits, 401(k) Plan benefits, stock benefits or any other employee benefits, or any other rights arising under federal, state or local laws prohibiting discrimination and/or harassment on the basis of race, color, age, religion, sexual orientation, religious creed, sex, national origin, ancestry, alienage, citizenship, nationality, mental or physical disability, denial of family and medical care leave, medical condition (including cancer and genetic characteristics), marital status, military status, gender identity, harassment or any other basis prohibited by law.

As a condition of the Company entering into this Agreement, Employee further represents that Employee has not filed against the Company or any of the other Releasees, any complaints, claims or lawsuits with any arbitral tribunal, administrative agency, or court prior to the date hereof, and that Employee has not transferred to any other person any such complaints, claims or lawsuits. Employee understands that by signing this Agreement, Employee waives her right to any monetary recovery in connection with a local, state or federal governmental agency proceeding and Employee waives her right to file a claim seeking monetary damages in any arbitral tribunal, administrative agency, or court. This Agreement does not: (i) prohibit or restrict Employee from communicating, providing relevant information to or otherwise cooperating with the U.S. Equal Employment Opportunity Commission or any other governmental authority with responsibility for the administration of fair employment practices laws (including with respect to SEC Whistleblowing) regarding a possible violation of such laws or responding to any inquiry from such authority, including an inquiry about the existence of this Release or its underlying facts, or (ii) require Employee to notify the Company of such communications or inquiry. Furthermore, notwithstanding the foregoing, this Release does not include and will not preclude: (a) rights or claims to vested benefits under any applicable retirement and/or pension plans; (b) rights under the Consolidated Omnibus Budget Reconciliation Act of 1985 ("COBRA"); (c) claims for unemployment compensation; (d) rights to defense and indemnification or under the Company's directors' and officers' liability insurance, if any, from the Company for actions or inactions taken by Employee in the course and scope of Employee's employment with the Company and its parents, subsidiaries and/or affiliates; (e) any rights Employee may have to obtain contribution as permitted by law in the event of entry of judgment against the Company as a result of any act or failure to act for which Employee and the Company are held jointly liable; (f) any rights to vested equity that vested prior to or because of the termination of Employee's employment and rights as a stockholder; and/or (g) any actions to enforce this Agreement.

For the avoidance of doubt, notwithstanding anything to the contrary, this Release does not limit Employee's right to receive an award from any governmental agency for information provided to the governmental agency. However, by executing this Release, Employee hereby waives the right to recover any damages, compensation or monetary award from the Company in any lawsuit or any proceeding before any governmental agency that arises out of alleged facts or circumstances on or before the effective date of this Release. Employee acknowledges that, in signing this Release, Employee has not relied on any promises or representations, express or implied, other than those that are set forth expressly herein.

4. Supplemental Release of Claims. In consideration for the payments, benefits and other promises and covenants set forth in this Agreement, following the Termination Date, Employee shall execute and deliver the Supplemental Release.

5. Covenant Not To Sue. Releasors warrant and represent that as of the date the Employee executes this Agreement (the "***Execution Date***"), none of them has filed any complaint, charge or lawsuit or commenced any other proceeding regarding the claims which are released by this Agreement with any federal, state or local court or any federal, state or local governmental agency or commission (a "Governmental Agency") or arbitrator, mediator or other dispute resolution process and that to the extent permitted by law (as explained further below) and consistent with this Agreement, they will not at any time hereafter file any complaint or lawsuit regarding the claims which are released by this Agreement with any court or Governmental Agency or arbitrator, mediator or other dispute resolution process, and if any such complaint or lawsuit is filed that is covered by this Agreement or the Supplemental Release, it will be immediately dismissed with prejudice as soon as possible thereafter. The Company's obligations under this Agreement are contingent upon the dismissal and withdrawal of any and all complaints, claims or actions regardless of where they may be pending. Should Employee breach any of the terms of this Agreement, to the extent authorized by law, Employee will be responsible for payment of all reasonable attorneys' fees and costs that the Company Parties incur in the course of enforcing the terms of the Agreement, including demonstrating the existence of a breach and any other contract enforcement efforts.

6. Non-Disparagement; References.

a. Employee agrees to that she shall not disparage, criticize, defame, slander, or otherwise take any action, whether in writing, verbally, or by any other non-verbal gesture or form of communication, with intent to: (i) harm the Company Parties; (ii) portray the Company Parties in an unfavorable light; or (iii) subject the Company Parties to scorn or ridicule.

b. The Company shall direct its directors and officers not to disparage, criticize, defame, or slander, or otherwise take any action, whether in writing or verbally, with intent to: (i) harm the Employee; (ii) portray the Employee in an unfavorable light; or (iii) subject the Employee to scorn or ridicule.

c. Subject to Section 6(d) below, the Company in response to an inquiry by a prospective employer will provide Employee with a neutral reference, which means that it will only provide the Employee's job title, dates of employment and, if requested by the Employee, Employee's salary, and further, the Company shall not contest any application Employee makes for unemployment benefits; provided, however, that nothing in this Section 6.b shall prohibit the Company from making any necessary disclosures about Employee, including regarding Employee's employment and Employee's separation of employment in connection with any judicial, administrative or other proceeding or investigation or as otherwise required by law.

d. Notwithstanding anything to the contrary in Section 6(c), the Company acknowledges that if a third party asks Mark Pruzanski, Chief Executive Officer of the Company, to be a reference for Employee, the Company shall use reasonable best efforts to cause Dr. Pruzanski to provide what he reasonably believes to be positive examples of Employee's performance and Employee's contributions to the Company as an employee.

e. The Company and the Employee shall mutually draft an official statement to be released to the press attached as Exhibit C.

7. Additional Acknowledgements and Agreements.

a. Employee understands and acknowledges that Employee remains bound by any and all agreements with the Company with regard to confidential information, assignment of rights in intellectual property, non-competition and non-solicitation that by their terms remain in effect notwithstanding the termination of employment. Without limiting the foregoing, Employee acknowledges and agrees that Employee's Invention, Non-Disclosure, and Non-Solicitation Agreement, a copy of which is attached hereto as Exhibit D (the "Restrictive Covenant Agreement") shall continue to remain in full force and effect pursuant to its terms and that Employee shall honor them.

b. Employee further agrees that Employee will not, directly or indirectly, make any disclosure of the Company's confidential information to anyone or make any use of confidential information on Employee's own behalf or on behalf of any third party, without the Company's prior written consent. Notwithstanding the foregoing, Employee understands that Employee may not be held criminally or civilly liable under any federal or state trade secret law for the disclosure of a trade secret that (A) is made (i) in confidence to a federal, state or local government official, either directly or indirectly, or to an attorney, and (ii) solely for the purpose of reporting or investigating a suspected violation of law, or (B) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal.

c. Employee agrees to permit the Company to examine any personal electronic devices that Employee owns that Employee has used in connection with Employee's employment with the Company, including, without limitation, any personal computers or smart phones. Employee further agrees that the Company has the right to remove any information pertaining to the Company or Employee's employment with the Company from such devices.

d. Employee agrees that Employee will not in any way communicate or discuss the terms of this Agreement, including but not limited to the amount paid to Employee, with any person other than Employee's spouse, attorney or tax advisor. Employee shall inform Employee's spouse, attorney and tax advisor of the confidential nature of this Agreement. The Company understands and agrees that the contents of the negotiations and discussions resulting in this Agreement shall be maintained as confidential and shall not be disclosed to any third parties, except to the extent required by federal or state law or as otherwise agreed to in writing with Employee.

e. Employee acknowledges that Employee has received payment in full for all services rendered in conjunction with Employee's employment by the Company, including payment for all wages, bonuses, and equity for any period before the Termination Date (other than any current salary and benefits due in the ordinary course in a final paycheck or thereafter), and that no other compensation is owed to Employee, including under Sections 5.2, 5.3 and 5.4 of the Employment Agreement with the Company, except as provided in the applicable provisions of Section 2 of this Agreement; provided, however that nothing herein shall affect any claims of entitlement Employee may have to vested benefits under any 401(k) plan or other ERISA-covered benefit plan (excluding severance) provided by the Company.

f. Employee acknowledges that as of the Execution Date, Employee has not contacted any Governmental Agency to report an alleged violation of applicable law by the Company, except to the extent Employee has already informed the Company in writing prior to the Execution Date.

g. Employee acknowledges that any breach of Section 8 will cause irreparable injury to the Company and that the Company, without the requirement of posting a bond or other security, may seek and obtain injunctive or other equitable relief against such breach or a threatened breach without prejudice to any other remedies that may be available to it.

8. Limitations Regarding Governmental Agency Activity. Notwithstanding anything in this Agreement and the Supplemental Release to the contrary, nothing in this Agreement, including the Supplemental Release, prohibits or restricts Employee from filing, or limits Employee's ability to file, a charge or complaint with a Governmental Agency; prohibits or restricts Employee from communicating with, providing documents or other relevant information to or otherwise cooperating with, or limit Employee's ability to communicate with, provide documents or other relevant information to or otherwise to cooperate with, any Governmental Agency, including, but not limited to, responding to any inquiry from such authority, including an inquiry about the existence of this Agreement, its release or its underlying facts. To the maximum extent permitted by law, however, nothing in this Agreement or the Supplemental Release shall be deemed to limit the Company's right to seek immediate dismissal of a charge or complaint on the basis that Employee's signing of this Agreement and the Supplemental Release constitutes a full release of any claims, including claims of discrimination, or to seek restitution to the extent permitted by law of the economic benefits provided to Employee under this Agreement in the event that Employee successfully challenge the validity of the Supplemental Release, provided, however, that Employee retains the right to receive, and the Company shall not seek restitution of, an award for information lawfully provided to a Governmental Agency.

9. Indemnification. The Company together with its its successors shall indemnify, defend and hold harmless Employee against all claims, actions, proceedings, demands, losses, damages, liabilities, costs and expenses (including, without limitation, attorneys' fees) (together, "Losses") to the extent the same arise from the conduct of the business of the Company or its subsidiaries, and whether arising prior to or following the date hereof, except any Losses caused by self-dealing, fraud, gross negligence, willful misconduct by Employee, or as otherwise prohibited by applicable law. In connection therewith, the Company or its successors shall advance to Employee reasonable attorneys' fees and expenses as such fees and expenses are incurred (subject to an undertaking from Employee to repay such advances if it shall be finally determined by a judicial decision which is not subject to further appeal that Employee was not entitled to the reimbursement of such fees and expenses), and Employee will be entitled to the protection of any insurance policies that either the Company or an applicable Company Party may elect to maintain generally for the benefit of their employees, officers and directors, to the extent as provided under such policies. This Section 9 shall survive the termination of the Employee's employment with the Company and this Agreement.

10. Disclaimer. This Agreement in no way constitutes an implicit or explicit admission or recognition by either party hereto of a violation of any federal, state, municipal, or local law.

11. Tax Provision. Employee acknowledges that Employee is not relying upon advice or representation of the Company with respect to the tax treatment of any of the payments or benefits provided by the Company. The benefits provided to Employee are intended to be exempt from or compliant with Section 409A of the Internal Revenue Code of 1986. *The Company makes no representation or warranty and shall have no liability to Employee or to any other person if any of the provisions of the Agreement are determined to constitute deferred compensation subject to Section 409A but not to satisfy an exemption for, or the conditions of, that section.* All payments under this Agreement will be reduced by all applicable taxes and withholdings.

12. Binding Agreement. This Agreement in its entirety shall be binding upon the parties hereto, their heirs, successors, legal representatives, and assigns.

13. Governing Law. The laws of the State of New York shall govern the interpretation and performance of this Agreement (without regard to New York's principles of conflicts of law) should any dispute arise concerning or related to this Agreement, except whereas otherwise expressly provided in this Agreement. In the event of any dispute arising out of this Agreement or any action to enforce the terms of this Agreement, the parties expressly submit to jurisdiction and venue in the state or federal courts of New York. Further, the parties expressly consent to accept service of any pleading or motion related to enforcing this Agreement by the prosecuting/moving party by mailing, hand delivering, or overnight expressing a copy to the other party and the other party's attorneys, if any.

14. Amendment. This Agreement may be amended or modified only by a written instrument executed by both the Company and Employee.

15. No Waiver. No delay or omission by the Company in exercising any right under this Agreement shall operate as a waiver of that or any other right. A waiver or consent given on any one occasion shall be effective only in that instance and shall not be construed as a bar or waiver of any right on any other occasion.

16. Severability. Whenever possible, each provision of this Agreement shall be interpreted in such a manner as to be effective and valid under applicable law, but if any provision of this Agreement shall be prohibited by or be invalid under law, such provision shall be effective to the extent not affected by such prohibition or invalidity, without invalidating or rendering unenforceable the remainder of such provision or the remaining provisions of this Agreement, and if this Agreement or the Supplemental Release is found to be unenforceable, this entire Agreement shall be void and the Company shall have no further obligation to Employee.

17. Headings for Reference. The Section headings in this Agreement are for convenience of reference only and have no independent legal significance.

18. Execution and Delivery. This Agreement may be executed and delivered in two or more counterparts, each of which, when so executed and delivered, shall be the original, but such counterparts together shall constitute but one of the same instrument. Delivery by Employee to the Company shall be effective provided it is made within twenty-one (21) days of the date Employee receives this Agreement by e-mail or regular mail. If delivery by Employee is effectuated by e-mail, it shall be scanned and e-mailed to the following address: david.ford@interceptpharma.com. In the case of e-mail delivery, Employee shall also send an original by regular mail to:

David Ford
Chief Human Resources Officer
Intercept Pharmaceuticals, Inc.
10 Hudson Yards, 37th Floor
New York, NY 10001

19. Entire Agreement. This Agreement (including the Supplemental Release) sets forth the entire agreement of the parties, there being no other promise or inducement to or for the execution of this Agreement other than the consideration cited above. Except as otherwise expressly set forth in this Agreement (including the continued applicability of Restrictive Covenant Agreement), this Agreement supersedes any and all prior agreements between Employee and the Company, whether written or oral. Employee affirms that Employee has not relied on any promises or representations, express or implied, other than those that are set forth expressly in this Agreement and that are intended to survive separation from employment, in accordance with the terms of the Agreement.

20. Release Acknowledgements. Employee acknowledges that:

a. Employee has carefully read and understand this Agreement and the Release;

b. The Company advised Employee to consult with an attorney and/or any other advisors of my choice before signing this Agreement;

c. Employee understands that this Agreement is **LEGALLY BINDING** and by signing it Employee gives up certain rights;

d. Employee has voluntarily chosen to enter into this Agreement and has not been forced or pressured in any way to sign it;

e. Employee acknowledges and agrees that the Separation Benefits are contingent on execution of this Agreement, which releases all of my claims against the Company and the Releasees, and Employee **KNOWINGLY AND VOLUNTARILY AGREES TO RELEASE** the Company and the Releasees from any and all claims Employee may have, known or unknown, in exchange for the benefits Employee will obtain by signing this Agreement and the Supplemental Release, and that these benefits are in addition to any benefit Employee would have otherwise received if Employee did not sign this Agreement;

f. Employee has seven (7) days after Employee signs this Agreement to revoke it by notifying the Company in writing. This Agreement (and the Release) will not become effective or enforceable until the seven (7) day revocation period has expired. This Agreement shall be effective and irrevocable on the eighth day following Employee's signing of this Agreement without recession.

g. This Agreement includes a **WAIVER OF ALL RIGHTS AND CLAIMS** Employee may have under the Age Discrimination in Employment Act of 1967 (29 U.S.C. §621 *et seq*.); and

h. This Release does not waive any rights or claims that may arise after this Agreement becomes effective, which is seven (7) days after Employee signs it, provided that Employee does not exercise my right to revoke this Agreement.

[Remainder of Page Intentionally Left Blank; Signature Page Follows]

IN WITNESS WHEREOF, the parties have executed this instrument on the dates indicated below.

/s/ Rachel McMinn	11/03/2017
Rachel McMinn	Date

INTERCEPT PHARMACEUTICALS, INC.

Signature:	/s/ David Ford
Name:	David Ford
Title:	Chief Human Resources Officer
Date:	11/01/2017

EXHIBIT A
SUPPLEMENTAL RELEASE OF CLAIMS

FOR AND IN CONSIDERATION OF the payments and benefits (the "Separation Benefits") to be provided to me in connection with the separation of my employment, in accordance with the Separation Agreement between Intercept Pharmaceuticals, Inc. (the "Company") and me dated as of November 1, 2017 (the "Agreement"), which Separation Benefits are conditioned on my signing this Supplemental Release of Claims ("Release") and which I will forfeit unless I execute and do not revoke this Release, I, on my own behalf and on behalf of my heirs and estate, voluntarily, knowingly and willingly release and forever discharge the Company, its subsidiaries, affiliates, parents, and, in their capacities as such, stockholders, together with each of those entities' respective officers, directors, stockholders, employees, agents, fiduciaries and administrators, each in their capacities as such (collectively, the "Releasees") from any and all claims and rights of any nature whatsoever which I now have or in the future may have against them up to the date I execute this Release, whether known or unknown, suspected or unsuspected. This Release includes, but is not limited to, any rights or claims relating in any way to my employment relationship with the Company or any of the other Releasees or the termination thereof, any contract claims (express or implied, written or oral), including, but not limited to, the Agreement, or any rights or claims under any statute, including, without limitation, the Americans with Disabilities Act, the Age Discrimination in Employment Act, the Older Workers' Benefit Protection Act, the Rehabilitation Act of 1973 (including Section 504 thereof), Title VII of the 1964 Civil Rights Act, the Civil Rights Act of 1866 (42 U.S.C. § 1981), the Civil Rights Act of 1991, the Equal Pay Act, the National Labor Relations Act, the Worker Adjustment and Retraining Notification Act, the Family Medical Leave Act, the Lilly Ledbetter Fair Pay Act, the Genetic Information Non-Discrimination Act, the New York State Human Rights Law, the New York City Human Rights Law, and the Employee Retirement Income Security Act of 1974, all as amended, and any other federal, state or local law. This Release specifically includes, but is not limited to, any claims based upon the right to the payment of wages, incentive and performance compensation, bonuses, equity grants, vacation, pension benefits, 401(k) Plan benefits, stock benefits or any other employee benefits, or any other rights arising under federal, state or local laws prohibiting discrimination and/or harassment on the basis of race, color, age, religion, sexual orientation, religious creed, sex, national origin, ancestry, alienage, citizenship, nationality, mental or physical disability, denial of family and medical care leave, medical condition (including cancer and genetic characteristics), marital status, military status, gender identity, harassment or any other basis prohibited by law.

As a condition of the Company entering into this Release, I further represent that I have not filed against the Company or any of the other Releasees, any complaints, claims or lawsuits with any arbitral tribunal, administrative agency, or court prior to the date hereof, and that I have not transferred to any other person any such complaints, claims or lawsuits. I understand that by signing this Release, I waive my right to any monetary recovery in connection with a local, state or federal governmental agency proceeding and I waive my right to file a claim seeking monetary damages in any arbitral tribunal, administrative agency, or court. This Release does not: (i) prohibit or restrict me from communicating, providing relevant information to or otherwise cooperating with the U.S. Equal Employment Opportunity Commission or any other governmental authority with responsibility for the administration of fair employment practices laws (including with respect to SEC Whistleblowing) regarding a possible violation of such laws or responding to any inquiry from such authority, including an inquiry about the existence of this Release or its underlying facts, or (ii) require me to notify the Company of such communications or inquiry. Furthermore, notwithstanding the foregoing, this Release does not include and will not preclude: (a) rights or claims to vested benefits under any applicable retirement and/or pension plans; (b) rights under the Consolidated Omnibus Budget Reconciliation Act of 1985 ("COBRA"); (c) claims for unemployment compensation; (d) rights to defense and indemnification or under the Company's directors' and officers' liability insurance, if any, from the Company for actions or inactions taken by me in the course and scope of my employment with the Company and its parents, subsidiaries and/or affiliates; (e) any rights I may have to obtain contribution as permitted by law in the event of entry of judgment against the Company as a result of any act or failure to act for which I and the Company are held jointly liable; (f) any rights to vested equity that vested prior to or because of the termination of my employment and rights as a stockholder; and/or (g) any actions to enforce the Agreement.

For the avoidance of doubt, notwithstanding anything to the contrary, this Release does not limit my right to receive an award from any governmental agency for information provided to the governmental agency. However, by executing this Release, I hereby waive the right to recover any damages, compensation or monetary award from the Company in any lawsuit or any proceeding before any governmental agency that arises out of alleged facts or circumstances on or before the effective date of this Release.

I acknowledge that, in signing this Release, I have not relied on any promises or representations, express or implied, other than those that are set forth expressly herein or in the Agreement and that are intended to survive separation from employment, in accordance with the terms of the Agreement.

Nondisclosure; Continuing Obligations - I understand and agree that, to the extent permitted by law, the terms and contents of this Release (as modified before signature) and the contents of the negotiations and discussions resulting in this Release shall be maintained as confidential by me and must not be disclosed to anyone other than a member of my immediate family, my attorney, accountant or other advisor (and, even as to such a person, only if the person agrees to honor this confidentiality requirement) except to the extent required by federal or state law or as otherwise agreed to in writing by the Company. I acknowledge and reaffirm my obligation to keep confidential and not disclose any and all non-public information concerning the Company that I acquired during the course of my employment or other relationship with the Company, including any non-public information concerning the Company's business affairs, business prospects and financial condition, as is stated more fully in any Invention, Non-Disclosure, and Non-Solicitation Agreement and that I will comply with such agreement in all other respects.

The Company understands and agrees that the contents of the negotiations and discussions resulting in this Release shall be maintained as confidential and shall not be disclosed to any third parties, except to the extent required by federal or state law or as otherwise agreed to in writing with me.

Return of Company Property - I confirm that I have returned to the Company in good working order all Company-owned keys, files, records (and copies thereof), equipment (including computer hardware, software and printers, wireless handheld devices, cellular phones, tablets, smartphones, etc.), Company identification, the Company proprietary and confidential information, and any other Company-owned property in my possession or control and I have left intact with, or delivered intact to, the Company all electronic Company documents and internal and external websites, including those that I developed or helped to develop during my employment, and that I have thereafter deleted, and destroyed any hard copies of, all electronic files relating to the Company that are in my possession or control, including any that are located on any of my personal computers or external or cloud storage. I further confirm that I have cancelled all accounts for my benefit, if any, in the Company's name including, but not limited to, credit cards, telephone charge cards, cellular phone and/or wireless data accounts and computer accounts. Notwithstanding the foregoing, I shall be permitted to retain my contacts and calendars and personal correspondence and any documents or data related to my compensation or reasonably needed for tax preparation purposes.

Final Compensation – I acknowledge that I have received payment in full for all services rendered in conjunction with my employment by the Company, including payment for all wages, bonuses, and equity for any period before the date of this Release (other than any current salary and benefits due in the ordinary course in a final paycheck or thereafter), and that no other compensation is owed to me, except as provided in the applicable provisions of Section 2 of the Agreement; *provided* that nothing herein shall affect any claims of entitlement I may have to vested benefits under any 401(k) plan or other ERISA-covered benefit plan (excluding severance) provided by the Company.

Cooperation – I agree to cooperate with, provide assistance to, and make myself reasonably available to the Company and its legal counsel in connection with any litigation (including arbitration or administrative hearings) or investigation or examination relating to the Company or any of its current or former employees, in which, in the reasonable judgment of the Company or its counsel, my assistance or cooperation is needed due to my personal involvement in or knowledge about the circumstances to which the litigation or investigation relates. I agree not to assist or provide information to any adverse party in any litigation against the Company or any of its current or former employees, except as required under law or formal legal process, unless I provide advance notice to the Company at least 10 days before such assistance or provision of information (or, if I am so required to assist or provide such information within less than 10 days of receipt of such requirement, after I provide timely advance notice to the Company) to allow the Company to take legal action with respect to the matter. Finally, I will undertake to satisfy requests for information from the Company with respect to the above undertaking. *Nothing in this Release is intended to restrict or preclude me from, or otherwise influence me in, testifying fully and truthfully in legal, administrative, or any other proceedings involving the Company, as required by law or formal legal process.*

Nature of Agreement – I understand and agree that this Release (which is attached to the Severance Agreement) is part of a severance agreement and does not constitute an admission of liability or wrongdoing on the part of the Company.

Voluntary Assent – I affirm that no other promises or agreements of any kind have been made to or with me by any person or entity whatsoever to cause me to sign this Release, other than as reflected in the Agreement and that I fully understand the meaning and intent of the Release. I acknowledge that, in signing this Release, I have not relied on any promises or representations, express or implied, other than those that are set forth expressly herein or in the Agreement and that are intended to survive separation from employment, in accordance with the terms of the Agreement. I further state and represent that I have carefully read this Release, understand the contents herein, freely and voluntarily assent to all of the terms and conditions hereof, and sign my name of my own free act.

Validity – Whenever possible, each provision of this Release shall be interpreted in such a manner as to be effective and valid under applicable law, but if any provision of this Release shall be prohibited by or be invalid under law, such provision shall be effective to the extent not affected by such prohibition or invalidity, without invalidating or rendering unenforceable the remainder of such provision or the remaining provisions of this Agreement, and if this Release is found to be unenforceable, the Agreement shall be void and the Company shall have no further obligation to me.

I further acknowledge that:

(1) I first received this Release on the date of the Agreement to which it is attached as Exhibit A;

(2) I understand that, in order for this Release to be effective, I may not sign it prior to the date of my separation of employment with the Company but that if I wish to receive the Separation Benefits, I must sign and return this Release prior to the thirtieth (30th) day following my separation of employment;

(3) I have carefully read and understand this Release;

(4) The Company advised me to consult with an attorney and/or any other advisors of my choice before signing this Release;

(5) I understand that this Release is **LEGALLY BINDING** and by signing it I give up certain rights;

(6) I have voluntarily chosen to enter into this Release and have not been forced or pressured in any way to sign it;

(7) I acknowledge and agree that the Separation Benefits are contingent on execution of this Release, which releases all of my claims against the Company and the Releasees, and I **KNOWINGLY AND VOLUNTARILY AGREE TO RELEASE** the Company and the Releasees from any and all claims I may have, known or unknown, in exchange for the benefits I have obtained by signing, and that these benefits are in addition to any benefit I would have otherwise received if I did not sign this Release;

(8) I have seven (7) days after I sign this Release to revoke it by notifying the Company in writing. The Release will not become effective or enforceable until the seven (7) day revocation period has expired. This Agreement shall be effective and irrevocable on the eighth day following my signing of this Agreement without recession.

(9) This Release includes a **WAIVER OF ALL RIGHTS AND CLAIMS** I may have under the Age Discrimination in Employment Act of 1967 (29 U.S.C. §621 *et seq*.); and

(10) This Release does not waive any rights or claims that may arise after this Release becomes effective, which is seven (7) days after I sign it, provided that I do not exercise my right to revoke this Agreement.

[Remainder of Page Intentionally Left Blank; Signature Page Follows]

Intending to be legally bound, I have signed this Release as of the date written below.

Signature: /s/Rachel McMinn — 01/05/2017

Rachel McMinn — Date Signed

Exhibit 10.21

Execution Version

TERMINATION OF LEASE

THIS TERMINATION OF LEASE (this "Agreement") is made as of the 31st day of December, 2017, by and between **ONE HUDSON YARDS OWNER LLC**, a Delaware limited liability company ("Landlord"), having an office at c/o Related Companies, 60 Columbus Circle, New York, New York 10023, and **INTERCEPT PHARMACEUTICALS, INC.**, a Delaware corporation ("Tenant"), having an office at 10 Hudson Yards, 37th Floor, New York, NY 10001.

W I T N E S S E T H:

WHEREAS, Landlord and Tenant entered into a Lease dated as of December 7, 2016 (the "Lease"), covering premises consisting of the entire 23rd through 25th floors of the building commonly known as 55 Hudson Yards, New York, New York (the "Building") and being more particularly described in the Lease (the "Premises");

WHEREAS, Tenant has requested that the Lease be terminated;

WHEREAS, Tenant's remaining obligations to Landlord under the Lease for the remainder of the term thereof are herein collectively referred to as the "Obligations"; and

WHEREAS, Landlord has agreed to Tenant's request to terminate the Lease as of December 31, 2017 (the "Termination Date"), in consideration of Landlord's receipt of the Termination Fee and the other covenants contained herein, which all of the parties hereto agree constitutes fair consideration for the transactions hereunder.

NOW, THEREFORE, for and in consideration of the mutual agreements contained herein and other good and valuable consideration received, Landlord and Tenant agree as follows (all capitalized terms used, but not defined herein, shall have the meanings assigned to them in the Lease):

1. **Termination of Lease.** (a) Landlord and Tenant hereby agree that, effective as of the Termination Date, the Lease and the term thereof shall terminate and expire, and Tenant's estate in and right of possession to the Premises shall terminate and be wholly extinguished, as if said Termination Date was originally set forth in the Lease as the expiration date thereunder. Effective as of the Termination Date, neither Landlord nor Tenant shall have any further rights or obligations under the Lease, except as provided in this Agreement. Effective as of the Termination Date, Landlord and Tenant for themselves and their predecessors-in-interest, successors and assigns, do hereby release and forever discharge each other, their successors and assigns, from all actions, causes of action, sums of money, covenants, agreements, promises, damages, judgments, claims and demands whatsoever in law or in equity which each against the other ever had, now has, or which they or their respective predecessors, successors or assigns hereafter may have, upon or by reason of any matter, cause or thing whatsoever from the beginning of the world through the Termination Date arising out of or in connection with the Lease or the Premises, or the Building; provided that (A) neither party shall be released from any of its obligations under this Agreement (and this Agreement shall survive the termination of the Lease), (B) neither Landlord or Tenant shall be released from any indemnification obligations that accrued under the Lease prior to the Termination Date and (C) the provisions of Section 8.13 and Section 8.21 of the Lease shall survive the termination of the Lease. Effective as of the Termination Date, Landlord shall be entitled to lease the Premises to any person or entity, or take any other action with respect thereto, free from any claim of Tenant or any person or entity claiming through Tenant.

(b) On or prior to the Termination Date, Tenant agrees to surrender unto Landlord and its successors and assigns, and Landlord agrees to accept, the Premises in its "as is" condition.

(c) In consideration of this Agreement and the termination of the Lease, Tenant agrees to permit the letter of credit in the amount of $8,698,662.00 issued by Citibank, N.A. (the "Letter of Credit") which Letter of Credit Landlord is presently holding as security under the Lease, to be drawn down for the payment of the following sums: (i) $7,800,000.00 (the "Termination Fee") to be drawn down and paid to Landlord in consideration of the termination of the Lease and the other transactions contemplated by this Agreement; and (ii) $898,662.00, representing the balance of the proceeds of the Letter of Credit shall be paid to Tenant. Tenant hereby authorizes Landlord to draw on the Letter of Credit and the entire proceeds of the Letter of Credit (the "Proceeds") and Landlord agrees to deliver Tenant's share of the Proceeds described in clause (ii) above to Tenant's bank account within three (3) Business Days of Landlord's receipt of the entire Proceeds in accordance with Tenant's wire instructions attached hereto as Exhibit A. Except as otherwise set forth in this Agreement, it is agreed that in no event shall Tenant at any time be entitled to receive any other sums from Landlord in connection with the Lease, including, without limitation, all or any portion of the Work Allowance or any reimbursement of any amounts previously paid by Tenant to Landlord in connection with the construction of the Terrace Space. Contemporaneously herewith, Landlord shall deliver a sight draft to the issuer of the Letter of Credit in order to obtain payment of the Proceeds, which sight draft shall provide for the Proceeds to be paid to Landlord's bank account, as designated by Landlord. Tenant hereby agrees to cooperate with Landlord and execute any and all documents required by the issuing bank in order to facilitate Landlord's efforts to draw down on the Proceeds of the Letter of Credit. The effectiveness of the surrender and termination provided for in this Agreement is subject to, and conditioned upon, Landlord's receipt of the Termination Fee in accordance with the terms hereof. If Landlord does not receive the Termination Fee in accordance with the terms hereof, then the termination of the Lease shall automatically be null and void and of no further force or effect and the Lease shall continue in full force and effect as if this Agreement had never been entered into.

(d) Tenant shall be responsible for, and shall indemnify Landlord for, any and all transfer taxes, sales taxes or other taxes or similar charges imposed by any federal, state or local governmental authority or under any Law arising from or relating to this Agreement, the Termination Fee or any of the other transactions hereunder. Tenant will execute and deliver to Landlord a New York State Form TP 584 and a New York City Form RPT.

(e) Landlord and Tenant agree that the disgorgement of any portion of the Termination Fee or the avoidance in whole or in part of this Agreement, under any applicable law, including, but not limited to, chapter 5 of title 11 of the United States Code (the "Bankruptcy Code"), shall be considered a breach of this Agreement by Tenant and shall entitle Landlord to seek the full amount of the Obligations and any other damages to which Landlord is entitled under the Lease from Tenant resulting from the breach of this Agreement.

2. **No Encumbered Property.** (a) Tenant represents and warrants to Landlord that (a) neither the Lease, the Letter of Credit, the Premises nor any Tenant's Property have been or will be mortgaged, pledged or otherwise encumbered in any way whatsoever, (b) Tenant is the holder of the entire lessee's interest in and to the Lease and Tenant has not assigned or otherwise transferred the same and Tenant has the right to surrender all of the same, and (c) Tenant has the full right, power and authority to enter into this Agreement without the consent of any person or entity.

(b) Landlord represents and warrants to Tenant that (a) Landlord is the holder of the entire lessor's interest in and to the Lease and Landlord has not assigned or otherwise transferred the same, and (b) Landlord has the full right, power and authority to enter into this Agreement without the consent of any person or entity (including, without limitation the holder of any mortgage encumbering the Landlord's interest in the Building or any other senior encumbrance).

(c) In addition to any other rights which the parties may have under the Lease, or at law or in equity, and not as a limitation therefore, Landlord and Tenant agree to indemnify and hold the other harmless from any loss or damage arising directly from the breach of the foregoing warranties and representations.

3. **Sublets, Licenses, and Occupancy.** Tenant represents and warrants to Landlord that neither the Premises nor any portion thereof has been sublet, licensed nor has any person or entity been granted any right to occupy the same.

4. **Access**. Notwithstanding anything to the contrary contained in the Lease, from and after the execution hereof, Landlord shall have the right, at any time, to enter upon and access the Premises in order to show the same to prospective tenants, purchasers or lenders.

5. **Brokers.** Landlord and Tenant represent and warrant that they have not dealt with any real estate agent or broker in connection with the negotiation, execution or delivery of this Agreement other than CBRE, Inc. (representing Landlord) ("Landlord's Broker") and Newmark & Company Real Estate, Inc., d/b/a Newmark Grubb Knight Frank (representing Tenant) ("Tenant's Broker"). Tenant shall defend, indemnify and hold Landlord harmless from and against any claims or demands for any commissions, finder's fees and/or other compensation (other than with respect to Landlord's Broker) arising out of any breach of the foregoing. Landlord shall defend, indemnify and hold Tenant harmless from and against any claims or demands for any commissions, finder's fees and/or other compensation (other than with respect to Tenant's Broker) arising out of any breach of the foregoing. Tenant shall enter into a separate agreement with Tenant's Broker which provides that, if this Agreement is executed and delivered by both Landlord and Tenant, Tenant shall pay to Tenant's Broker any commission that Tenant's Broker may be entitled to under such separate agreement (if any), in accordance with the terms and conditions of such agreement.

6. **Entire Agreement; Modifications; Invalidity; Counterparts.** This Agreement contains the entire understanding of the parties with respect to the subject matters covered hereby and may be modified only by a written instrument executed by the parties hereto. Landlord and Tenant intend that, to the maximum extent legally possible, the invalidity or unenforceability of any provision of this Agreement will not affect any of the other provisions hereof. This Agreement may be executed in multiple counterparts, each of which shall constitute an original, even where such executed counterpart is delivered via facsimile or Portable Document Format, but all of which, when taken together, shall constitute one and the same instrument.

7. **Binding Effect; Governing Law; Notices.** This Agreement shall be binding upon and inure to the benefit of the parties hereto and their respective successors and assigns. This Agreement shall be governed by the laws of the State of New York (without giving effect to conflict of laws principles thereof). Any notices, demands or other correspondence to be sent hereunder shall be given in accordance with Section 8.01 of the Lease.

8. **Time of the Essence.** Time shall be of the essence with respect to all dates contained herein.

9. **Survival.** The representations, warranties, covenants, liabilities, indemnities and other obligations of each party contained in or arising under this Agreement shall survive the termination of the Lease.

10. **Further Assurances.** Each party agrees that it shall promptly execute and deliver to the other party such other instruments as the other party shall reasonably request in order to further evidence or effectuate the agreements hereunder.

[REMAINDER OF THIS PAGE INTENTIONALLY LEFT BLANK]

IN WITNESS WHEREOF, Landlord and Tenant have duly executed this Agreement effective as of December 31, 2017.

ONE HUDSON YARDS OWNER LLC

By: /s/ Andrew Rosen
Name: Andrew Rosen
Title: Authorized Signatory

INTERCEPT PHARMACEUTICALS, INC.

By: /s/ Jerome Durso
Name: Jerome Durso
Title: C.O.O.

Exhibit 12.1

CONSOLIDATED RATIOS OF EARNINGS TO FIXED CHARGES

We did not record earnings for the years ended December 31, 2017, 2016, 2015, 2014, or 2013. Accordingly, our earnings were inadequate to cover fixed charges for each period. The amount of the deficiency by which our earnings did not cover our fixed charges for each such period is disclosed in the table below.

	Years Ended December 31,				
	2017	2016	2015	2014	2013
			(in thousands)		
Deficiency	$ (360,367)	$ (412,830)	$ (226,429)	$ (283,226)	$ (67,792)

For purposes of calculating the ratio of earnings to fixed charges, earnings are calculated as follows: (i) adding (a) pretax income (loss) from continuing operations; (b) fixed charges; (c) amortization of capitalized interest: (d) distributed income of equity investees; and (e) our share of pretax losses of equity investees for which charges arising from guarantees are included in fixed charges; and (ii) then subtracting from such sum (A) interest capitalized; and (B) any net income attributable to non-controlling interests. Fixed charges are calculated as the sum of (1) interest costs (both expensed and capitalized); (2) amortization of debt expense and discount or premium relating to any indebtedness; and (3) that portion of rental expense that is representative of the interest factor.

Exhibit 21.1

SUBSIDIARIES OF INTERCEPT PHARMACEUTICALS, INC.

Intercept Italia S.r.l, an Italian entity

Intercept Pharma Europe Ltd., a United Kingdom entity

Intercept Pharma UK & Ireland Ltd, a United Kingdom entity

Intercept Pharma Ltd, a United Kingdom entity

Intercept Pharma Canada, Inc., a Canadian entity

Intercept Pharma Switzerland GmbH, a Swiss entity

Intercept Pharma Deutschland GmbH, a German entity

Intercept Pharma France SAS, a French entity

Intercept Pharma Austria GmbH, an Austrian entity

Intercept Pharma Spain, S.L.U., a Spanish entity

Intercept Pharma Portugal Unipessoal Lda., a Portuguese entity

Intercept Pharma Danmark ApS, a Danish entity

Intercept Pharma Nederland B.V., a Dutch entity

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 on Form S-8 (No. 333 184810, No. 333-188064, and No. 333-206247) and Form S-3 (No. 333-194974) of Intercept Pharmaceuticals, Inc. of our reports dated February 28, 2018, with respect to the consolidated balance sheets of Intercept Pharmaceuticals, Inc. as of December 31, 2017 and 2016, and 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, 2017, and the related notes (collectively, the "consolidated financial statements"), and the effectiveness of internal control over financial reporting as of December 31, 2017, which reports appear in the December 31, 2017 annual report on Form 10-K of Intercept Pharmaceuticals, Inc.

/s/ KPMG LLP

New York, New York
February 28, 2018

Exhibit 31.1

CERTIFICATIONS UNDER SECTION 302

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 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 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: February 28, 2018

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

Exhibit 31.2

CERTIFICATIONS UNDER SECTION 302

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 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 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: February 28, 2018

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

Exhibit 32

CERTIFICATIONS UNDER SECTION 906
OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to section 906 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of section 1350, chapter 63 of title 18, United States Code), each of the undersigned officers of Intercept Pharmaceuticals, Inc., a Delaware corporation (the "Company"), does hereby certify, to such officer's knowledge, that:

The Annual Report for the year ended December 31, 2017 (the "Form 10-K") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: February 28, 2018 /s/ Mark Pruzanski
Mark Pruzanski, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Dated: February 28, 2018 /s/ Sandip Kapadia
Sandip Kapadia
Chief Financial Officer
(Principal Financial and Accounting Officer)