

INTERCEPT PHARMACEUTICALS INC
Form 424B5
June 29, 2016

The information in this preliminary prospectus supplement and the accompanying prospectus is not complete and may be changed. A registration statement relating to the notes has become effective under the Securities Act of 1933, as amended. This preliminary prospectus supplement is not an offer to sell the notes and it is not soliciting an offer to buy the notes in any jurisdiction where the offer or sale is not permitted.

**Filed Pursuant to Rule 424(b)(5)
Registration No. 333-194974**

SUBJECT TO COMPLETION, DATED JUNE 29, 2016

**PRELIMINARY PROSPECTUS SUPPLEMENT
(To prospectus dated April 1, 2014)**

\$400,000,000

INTERCEPT PHARMACEUTICALS, INC.

% Convertible Senior Notes due 2023

We are offering \$400,000,000 principal amount of our % Convertible Senior Notes due 2023 (the notes). The notes will bear interest at a rate of % per year, payable semiannually in arrears on January 1 and July 1 of each year, beginning on January 1, 2017. The notes will mature on July 1, 2023.

Holders may convert their 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 (the measurement period) in which the trading price (as defined below) per \$1,000 principal amount of 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 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 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, as described in this prospectus supplement.

The conversion rate will initially be _____ shares of common stock per \$1,000 principal amount of notes (equivalent to an initial conversion price of approximately \$ _____ 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 notes in connection with such a corporate event in certain circumstances.

We may not redeem the notes prior to July 6, 2021. We may redeem for cash all or any portion of the 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 notes to be redeemed, *plus* accrued and unpaid interest to, but excluding, the redemption date.

No sinking fund is provided for the notes.

If we undergo a fundamental change, holders may require us to repurchase for cash all or any portion of their notes at a fundamental change repurchase price equal to 100% of the principal amount of the notes to be repurchased, *plus* accrued and unpaid interest to, but excluding, the fundamental change repurchase date.

The notes will be our senior unsecured obligations and will rank senior in right of payment to our future indebtedness that is expressly subordinated in right of payment to the 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.

We do not intend to apply to list the notes on any securities exchange or any automated dealer quotation system. Our common stock is listed on The NASDAQ Global Select Market under the symbol ICPT. The last reported sale price of our common stock on The NASDAQ Global Select Market on June 28, 2016 was \$149.37 per share.

Investing in the notes involves a high degree of risk. See Risk Factors beginning on page S-19 of this prospectus supplement.

	Per Note	Total
Public offering price ⁽¹⁾	\$	\$
Underwriting discounts and commissions	\$	\$
Proceeds, before expenses, to us	\$	\$

(1) _____ Plus accrued interest, if any, from July _____, 2016.

We have granted the underwriters the right to purchase, exercisable within a 30-day period, up to an additional \$60,000,000 principal amount of notes, solely to cover over-allotments.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of the notes or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

We expect that delivery of the notes will be made to investors in book-entry form through The Depository Trust Company on or about July _____, 2016.

Joint Book-Running Managers

RBC Capital Markets
BofA Merrill Lynch

Citigroup
June , 2016

UBS Investment Bank
Credit Suisse

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

Neither we nor the underwriters have authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement, in the accompanying prospectus or in any free writing prospectus filed with the Securities and Exchange Commission by or on behalf of us or to which we have referred you. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus do not constitute an offer to sell, or a solicitation of an offer to purchase, the securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction to or from any person to whom or from whom it is unlawful to make such offer or solicitation of an offer in such jurisdiction. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and in any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of the date of those respective documents. It is important for you to read and consider all information contained in this prospectus supplement and in the accompanying prospectus, including the documents incorporated by reference herein and therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled *Where You Can Find More Information* and *Incorporation by Reference* in this prospectus supplement and in the accompanying prospectus.

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Unless the context otherwise indicates, references in this prospectus to we, our, us and the Company refer, collectively, to Intercept Pharmaceuticals, Inc., a Delaware corporation, and its consolidated subsidiaries.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements contained or incorporated by reference herein or therein regarding our strategy, future operations, financial position, future revenue, projected costs, prospects, plans and objectives of management and expected market growth, other than statements of historical facts, are forward-looking statements. The words anticipate, believe, estimate, expect, intend, may, plan, predict, project, potential, will, would, could, similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The forward-looking statements in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein include, among other things:

- our ability to successfully commercialize Ocaliva™ (obeticholic acid, or OCA) in primary biliary cholangitis, or PBC, and our ability to maintain our regulatory approval of Ocaliva in PBC in the United States;
- the initiation, cost, timing, progress and results of our development activities, preclinical studies and clinical trials;
- the timing of and our ability to obtain and maintain regulatory approval of OCA in PBC in countries outside the United States and in indications other than PBC and any other product candidates we may develop such as INT-767;
- conditions that may be imposed by regulatory authorities on our marketing approvals for our 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 approved product candidates;
 - our plans to research, develop and commercialize our product candidates;
 - our ability to obtain and maintain intellectual property protection for our product candidates;
- our ability to successfully commercialize OCA in indications other than PBC and our other product candidates;
- the size and growth of the markets for our 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 that we may receive for our products from payors;
 - the success of competing drugs that are or become available;
- the election by our collaborators to pursue research, development and commercialization activities;
 - our ability to attract collaborators with development, regulatory and commercialization expertise;
 - regulatory developments in the United States and other countries;
 - the performance of third-party suppliers and manufacturers;
 - our need for and ability to obtain additional financing;
- our estimates regarding expenses, future revenues and capital requirements and the accuracy thereof;
 - our use of cash, short-term investments and the proceeds from this offering; and
 - our ability to attract and retain key scientific or management personnel.

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We cannot guarantee that we actually will achieve the plans, intentions or expectations expressed or implied in our forward-looking statements. There are a number of important factors that could cause actual results, levels of activity, performance or events to differ materially from those expressed or implied in the forward-looking statements we make. These important factors include our critical accounting estimates described in Part II, Item 7 Management's Discussion and Analysis of Financial Condition and Results of Operations Critical Accounting Policies and Estimates of our Annual Report on Form 10-K for the fiscal year ended December 31, 2015 and our Quarterly Report on Form 10-Q for the quarter ended March 31, 2016, and the factors set forth under the caption Risk Factors in this prospectus supplement.

Any forward-looking statement speaks only as of the date on which it is made. Although we may elect to update forward-looking statements in the future, we specifically disclaim any obligation to do so, even if our estimates change. As a result, you should not rely on those forward-looking statements as representing our views as of any date subsequent to the date the statements were made.

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INDUSTRY AND MARKET DATA

This prospectus supplement contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. We obtained such industry and market data from our own research as well as from industry and general publications, surveys and studies conducted by third parties.

This data involves a number of assumptions and limitations and contains projections and estimates of the future performance of the industries in which we operate that are subject to a high degree of uncertainty. We caution you not to give undue weight to such projections, assumptions and estimates. Further, industry and general publications, studies and surveys generally state that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe that these industry and general publications, studies and surveys are reliable, we have not independently verified the data contained in them. In addition, while we believe that the results and estimates from our internal research are reliable, such results and estimates have not been verified by any independent source.

NON-GAAP FINANCIAL MEASURES

This prospectus supplement and the documents incorporated by reference herein present 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 the anticipated \$45 million net expense for the settlement of the purported securities class action lawsuit, 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. 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.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere in this prospectus supplement, the accompanying prospectus and in the documents we incorporate by reference. This summary does not contain all of the information you should consider before making an investment decision. You should read carefully this entire prospectus supplement, the accompanying prospectus and any related free writing prospectus, especially the risks of investing in the notes discussed under Risk Factors contained in this prospectus supplement, along with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus supplement and the accompanying prospectus.

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.

Our lead product, obeticholic acid, or 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.

OCA was approved in the United States in May 2016 for use in patients with primary biliary cholangitis, or PBC, under the brand name Ocaliva™. We commenced sales and marketing of Ocaliva shortly after receiving marketing approval in the United States, and the medicine is now available to patients primarily through our specialty commercial organization. In June 2015, we received notice of the acceptance of the Marketing Authorization Application, or MAA, for review by the European Medicines Agency, or EMA, for use of Ocaliva in PBC. If we are successful in the EMA review process, we anticipate receiving marketing approval in late 2016. We do not expect to generate significant sales revenues in 2016.

OCA is also being developed to treat a variety of other non-viral chronic liver diseases such as nonalcoholic steatohepatitis, or NASH, primary sclerosing cholangitis, or PSC, and biliary atresia. We are currently evaluating our future development strategy for OCA in other indications, for our product candidate INT-767 and for our pre-clinical candidates. The following chart shows the current stage of development of OCA for different patient populations and the preclinical programs for our other product candidates.

Our Marketed Product and Clinical/Pre-Clinical Pipeline

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OCA has been tested in five placebo-controlled clinical trials, including a Phase 3 clinical trial in patients with PBC and two Phase 2 clinical trials in patients with NASH or a precursor disease to NASH known as nonalcoholic fatty liver disease, or NAFLD. OCA met the primary efficacy endpoint in each of these trials with statistical significance. In addition, in October 2015, we announced results from a Phase 2 dose ranging trial of OCA in 200 patients with NASH in Japan conducted by our collaborator, Sumitomo Dainippon Pharma Co., Ltd., or Sumitomo Dainippon, which did not meet its primary endpoint with statistical significance. However, Sumitomo Dainippon has informed us that it is exploring the initiation of a Phase 3 clinical trial for OCA in NASH patients intended to support the registration of this indication in Japan. 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.

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 initiated our Phase 3 clinical trial in non-cirrhotic NASH patients with liver fibrosis, known as the REGENERATE trial, in September 2015. In December 2015, we initiated a Phase 2 clinical trial, known as the CONTROL trial, to characterize the lipid metabolic effects of OCA and cholesterol management effects of concomitant statin administration in NASH patients.

In addition to PBC and NASH, we continue to invest in research of OCA for additional patient populations with other liver diseases, including two Phase 2 trials for PSC and pediatric patients with biliary atresia, respectively. We have also initiated a Phase 1 trial in healthy volunteers for INT-767, a dual FXR and TGR5 agonist.

Our current patents for OCA are scheduled to expire at various times through 2033. Our current plan is to commercialize OCA ourselves in the United States and Europe for the treatment of PBC, NASH and other indications primarily by targeting physicians who specialize in the treatment of liver and intestinal diseases, including both hepatologists and gastroenterologists. We own worldwide rights to OCA except for Japan, China and Korea, where we have exclusively licensed OCA to Sumitomo Dainippon along with an option to exclusively license OCA in certain other Asian countries.

Ocaliva for PBC

PBC is a chronic autoimmune liver disease that, if inadequately treated, may eventually lead to cirrhosis, liver failure and death. In May 2016, Ocaliva received accelerated approval from the FDA 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. The accelerated approval was supported by the results of the pivotal Phase 3 POISE trial, which was completed in March 2014. We are currently conducting a Phase 4 confirmatory outcomes trial of Ocaliva, known as the COBALT trial, to support post-marketing regulatory requirements. Full approval from the FDA for Ocaliva for PBC may be contingent upon verification and description of clinical benefit in confirmatory trials.

Ocaliva was granted accelerated FDA approval based on a reduction in alkaline phosphatase, or ALP. 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. These represent the largest PBC clinical datasets assembled to analyze the correlation of biochemical therapeutic response with clinical outcomes in PBC patients.

According to our analysis of 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 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 currently are focusing our commercial efforts on PBC patients who have elevated ALP levels of at least 1.67 times the upper limit of

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normal, or ULN, despite receiving treatment with ursodiol and those who cannot tolerate ursodiol. We believe there are approximately 37,000 diagnosed PBC patients in our target markets who still have an ALP level of at least 1.67 times ULN after treatment on ursodiol who may currently be eligible for treatment with Ocaliva. 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 of at least ULN but less than 1.67 times ULN who may be treated with Ocaliva.

In June 2015, we received notice of the acceptance of the MAA for review by the EMA for use of OCA in PBC. If we are successful in the EMA review process, we anticipate receiving marketing approval in late 2016, with planned commercial launches thereafter in certain European countries. We also plan to apply for marketing approval of OCA in PBC in other markets across the world such as Canada and Australia.

We are commercializing Ocaliva in the United States using our internal commercial organization. We believe that our commercial organization is equipped to address more than 4,000 physicians, covering 70% to 80% of patients with PBC in the United States. We plan to address this target audience with our 45 sales representatives and six regional directors who are experienced in healthcare product sales. We have also hired a team of field-based medical science liaisons and expect that they will play an important role in providing medical information about Ocaliva to clinicians and other health care professionals. We have and plan to continue to build an internal 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.

OCA for NASH

NASH is a common and serious chronic liver disease caused by excessive fat accumulation in the liver, or steatosis, that induces inflammation and may lead to progressive fibrosis and cirrhosis, followed by eventual liver failure and death. In NASH patients, for reasons that are as yet not 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.

There are currently no drugs approved for the treatment of NAFLD or NASH. However, various therapeutics are 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. 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.

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 potent ability of OCA to activate FXR could result in a major clinical benefit through potential amelioration or reversal of liver fibrosis, inflammation, steatosis and insulin resistance.

Phase 2b FLINT Trial for NASH

OCA achieved the primary endpoint in the Phase 2b trial for the treatment of NASH, known as the FLINT trial, which was sponsored by the NIDDK, a part of the National Institutes of Health. 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. The results were subsequently published online in the *Lancet* in November 2014.

The percentage of patients meeting the FLINT primary histological endpoint, 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 (45% versus 21%, $p = 0.0002$, $n = 219$). Statistical significance is based on a p-value of less than 0.05. The mean pre-treatment baseline NAS for patients in the OCA treatment group was 5.3 of a total possible score of 8.0

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(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, elevated ALT, insulin resistance and severe obesity (each factor $p < 0.05$ for OCA compared to placebo based on 95% confidence interval of published odds ratios).

A significantly greater number of OCA-treated patients also achieved 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%, $p = 0.0018$). The NASH clinical research network fibrosis staging system was used to categorize the pattern of fibrosis and architectural remodeling of the liver: no fibrosis (F0), perisinusoidal or periportal fibrosis (F1), perisinusoidal and periportal fibrosis (F2), bridging fibrosis (F3) and cirrhosis (F4). Fibrosis sub-stages 1a, 1b and 1c were considered F1 for the analysis.

The secondary endpoint of NASH resolution, based on a global histological assessment, also showed improvement, although not statistically significant (22% versus 13%, $p = 0.0832$, 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%, $p = 0.0278$).

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 the 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 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

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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. 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.

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.

REGENERATE: Phase 3 Trial in NASH with Advanced Liver Fibrosis

In September 2015, we initiated the previously announced international Phase 3 trial of OCA in patients with non-cirrhotic NASH with advanced liver fibrosis, known as the REGENERATE trial, which is currently enrolling patients. 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 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 up to 300 qualified centers 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. The trial will include a pre-planned interim histology analysis after 72 weeks of treatment in 1,400 patients, which if successful 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. We expect to complete enrollment of the 1,400 in the first half of 2017. 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.

Two co-primary endpoints will be assessed in the interim analysis: (i) the proportion of OCA-treated patients relative to placebo achieving at least one stage of liver fibrosis improvement with no worsening of NASH and (ii) the proportion of OCA-treated patients relative to placebo achieving NASH resolution with no worsening of liver fibrosis.

The REGENERATE trial will also assess secondary outcome measures such as improvement of both fibrosis and NASH and the resolution of fibrosis.

Additional NASH Clinical Programs

In addition to the REGENERATE trial, we initiated a Phase 2 clinical trial, known as the CONTROL trial, to characterize the lipid metabolic effects of OCA and cholesterol management effects of concomitant statin administration in NASH patients in December 2015. We expect to complete enrollment by late 2016.

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Other Indications and Pipeline

In addition to PBC and NASH, we plan to continue our research of OCA in patient populations suffering from other liver diseases, as we believe that FXR activation has broad therapeutic potential. In December 2014, we initiated an international Phase 2 clinical trial, known as the AESOP trial, in patients with PSC to evaluate the effects of 24 weeks of treatment with varying doses of OCA compared to placebo. We anticipate completing enrollment for our AESOP trial by the end of 2016. In October 2015, we initiated a Phase 2 clinical trial, known as the CARE trial, of OCA in pediatric patients with biliary atresia. This trial will evaluate the effects of 11 weeks of OCA treatment where patients with biliary atresia will be randomized to varying doses of OCA or a control group receiving only their current treatment. As part of our development program, in November 2015, we initiated a Phase 1 clinical trial of our second product candidate to enter clinical development, called INT-767, a dual FXR and TGR5 agonist, in healthy volunteers. We anticipate completing this Phase 1 trial for INT-767 by the end of 2016. We are currently evaluating our future development strategy for OCA in other indications, for INT-767 and for our pre-clinical candidates.

Our Strategy

Our strategy is to develop and commercialize novel therapeutics for patients with non-viral, progressive 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, initially for the treatment of PBC;
- obtain marketing approval of OCA for the treatment of PBC in Europe and other target markets such as Canada and Australia;
- 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
- advance the development of earlier-stage product candidates in our pipeline.

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. We anticipate that we will continue to increase our product development, scientific, commercial and administrative personnel significantly in the United States and abroad as part of our longer-term growth strategy.

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Risks Related to Our Business

We are a biopharmaceutical company with a limited operating history as a commercial entity, and our business and ability to execute our business strategy are subject to a number of important risks of which you should be aware before you decide to invest in the notes. In particular, you should consider the following risks, which are discussed more fully in the section entitled "Risk Factors" in this prospectus supplement:

We are dependent on the successful commercialization of Ocaliva, which received accelerated approval in May 2016 from the FDA as a treatment for PBC. To the extent Ocaliva is not commercially successful, our business, financial condition and results of operations may be materially and adversely affected and the price of our common stock may decline.

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

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 developing product candidates for the treatment of rare diseases or diseases for which there are no or limited therapies 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.

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.

Reimbursement decisions by third-party payors may have an adverse effect on pricing and market acceptance of OCA or our other marketed products. If our products do not receive sufficient reimbursement or they are not covered at all, it is less likely that they will be widely used.

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

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

Company Information

We were incorporated in the State of Delaware on September 4, 2002. Our principal executive offices are located at 450 W. 15th Street, Suite 505, New York, New York 10011, and our telephone number is (646) 747-1000. We also have administrative offices in San Diego, California and London, United Kingdom. Our website address is www.interceptpharma.com. The information contained on or accessible through our website is not incorporated by reference into, and should not be considered part of, this prospectus supplement or the accompanying prospectus. We have included our website address in this prospectus supplement as an inactive textual reference only.

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THE OFFERING

The summary below describes the principal terms of the notes. Certain of the terms and conditions described below are subject to important limitations and exceptions. The Description of Debt Securities section of the accompanying prospectus, as supplemented by the Description of Notes section of this prospectus supplement, contains a more detailed description of the terms and conditions of the notes. As used in this section, we, our, and us refer to Intercept Pharmaceuticals, Inc. and not to its consolidated subsidiaries.

Issuer

Intercept Pharmaceuticals, Inc., a Delaware corporation.

Securities

\$400,000,000 principal amount of % Convertible Senior Notes due 2023 (*plus* up to an additional \$60,000,000 principal amount, solely to cover over-allotments).

Maturity

July 1, 2023, unless earlier repurchased, redeemed or converted.

Interest

% per year. Interest will accrue from July , 2016 and will be payable semiannually in arrears on January 1 and July 1 of each year, beginning on January 1, 2017. We will pay additional interest, if any, at our election as the sole remedy relating to the failure to comply with our reporting obligations as described under Description of Notes Events of Default.

Conversion Rights

Holders may convert all or any portion of their notes, in multiples of \$1,000 principal amount, 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:

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;

during the five business day period after any five consecutive trading day period (the measurement period) in which the trading price (as defined under Description of Notes Conversion Rights Conversion upon Satisfaction of Trading Price Condition) per \$1,000 principal amount of 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;

if we call any or all of the notes for redemption, at any time prior to the close of business on the scheduled trading day immediately preceding the redemption date; or

upon the occurrence of specified corporate events described under Description of Notes Conversion Rights Conversion upon Specified Corporate Events.

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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 all or any portion of their notes, in multiples of \$1,000 principal amount, at the option of the holder regardless of the foregoing circumstances.

The conversion rate for the notes is initially shares of common stock per \$1,000 principal amount of notes (equivalent to an initial conversion price of approximately \$ per share of common stock), subject to adjustment as described in this prospectus supplement.

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. If we satisfy our conversion obligation solely in cash or through payment and delivery, as the case may be, of a combination of cash and shares of our common stock, the amount of cash and shares of common stock, if any, due upon conversion will be based on a daily conversion value (as described herein) calculated on a proportionate basis for each trading day in a 20 trading day observation period (as described herein). See Description of Notes Conversion Rights Settlement upon Conversion.

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 notes in connection with such a corporate event in certain circumstances, as described under Description of Notes Conversion Rights Increase in Conversion Rate upon Conversion upon a Make-whole Fundamental Change.

You will not receive any additional cash payment or additional shares representing accrued and unpaid interest, if any, upon conversion of a note, except in limited circumstances. Instead, interest will be deemed to be paid by the 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 paid or delivered, as the case may be, to you upon conversion of a note.

Redemption at Our Option

We may not redeem the notes prior to July 6, 2021. We may redeem for cash all or part of the 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 notes to be redeemed, *plus* accrued and unpaid interest to, but excluding, the redemption date. No sinking fund is provided for the notes, which means that we are not required to redeem or retire the notes periodically.

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We will give notice of any redemption not less than 45 nor more than 60 calendar days before the redemption date by mail or electronic delivery to the trustee, the paying agent and each holder of notes. See Description of Notes Optional Redemption.

Fundamental Change

If we undergo a fundamental change (as defined in this prospectus supplement under Description of Notes Fundamental Change Permits Holders to Require Us to Repurchase Notes), subject to certain conditions, holders may require us to repurchase for cash all or part of their notes in minimum principal amounts of \$1,000 or an integral multiple thereof. The fundamental change repurchase price will be equal to 100% of the principal amount of the notes to be repurchased, *plus* accrued and unpaid interest to, but excluding, the fundamental change repurchase date. See Description of Notes Fundamental Change Permits Holders to Require Us to Repurchase Notes.

Ranking

The notes will be our senior unsecured obligations and will rank:

senior in right of payment to our future indebtedness that is expressly subordinated in right of payment to the 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.

As of March 31, 2016, we had no consolidated indebtedness and total consolidated liabilities of \$105.0 million, \$4.8 million of which were owed by our subsidiaries (including trade payables), to which the notes would have been structurally subordinated. After giving effect to the issuance of the notes (assuming no exercise of the underwriters over-allotment option), our total consolidated indebtedness and other liabilities would have been \$505.0 million as of March 31, 2016. The indenture governing the notes does not limit the amount of debt that we or our subsidiaries may incur.

Use of Proceeds

We estimate that the net proceeds from the sale of the notes in this offering will be approximately \$ million (or \$ million if the underwriters exercise their over-allotment option in full), after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

We expect to enter into capped call transactions with one or more of the underwriters or their respective affiliates (the option counterparties). We intend to use approximately

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\$ million of the net proceeds of this offering to pay the cost of the capped call transactions. We intend to use the remaining net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments, to fund:

the ongoing commercialization of Ocaliva in PBC in the United States;

our preparation for and, subject to receipt of marketing approval, potential initiation of the commercial launch of Ocaliva in PBC in certain European countries as well as other target markets across the world such as Canada and Australia;

the continued clinical development of OCA in PBC, NASH and PSC;

the advancement of our clinical program for INT-767; and

continued advancement of other preclinical pipeline and research and development programs.

The balance, if any, will be used for general corporate purposes, including general and administrative expenses, capital expenditures, working capital and prosecution and maintenance of our intellectual property. See Use of Proceeds.

If the underwriters exercise their over-allotment option, we may use a portion of the net proceeds from the sale of the additional notes to enter into additional capped call transactions.

Book-entry Form

The notes will be issued in book-entry form and will be represented by permanent global certificates deposited with, or on behalf of, The Depository Trust Company (DTC) and registered in the name of a nominee of DTC. Beneficial interests in any of the notes will be shown on, and transfers will be effected only through, records maintained by DTC or its nominee and any such interest may not be exchanged for certificated securities, except in limited circumstances.

Absence of a Public Market for the Notes

The notes are new securities and there is currently no established market for the notes. Accordingly, we cannot assure you as to the development or liquidity of any market for the notes. The underwriters have advised us that they currently intend to make a market in the notes. However, they are not obligated to do so, and they may discontinue any market making with respect to the notes without notice. We do not intend to apply for a listing of the notes on any securities exchange or any automated dealer quotation system.

U.S. Federal Income and Estate Tax Consequences

For the U.S. federal income and certain estate tax consequences of the holding, disposition and conversion of the notes, and the holding and disposition of shares of our common stock, see Material U.S. Tax Considerations. You should consult your tax advisor with respect to the application of U.S. federal

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income and estate tax laws in your particular situation, as well as the tax consequences arising under the laws of any state, local, foreign or other taxing jurisdiction or under any applicable tax treaty.

Capped Call Transactions

In connection with the pricing of the notes, we expect to enter into capped call transactions with the option counterparties. The capped call transactions are expected to reduce potential dilution to our common stock and/or offset any cash payments due in excess of the principal amount of converted notes, as the case may be, upon any conversion of notes, with such reduction and/or offset subject to a cap. If the underwriters exercise their over-allotment option, we may enter into additional capped call transactions.

In connection with establishing their initial hedge of the capped call transactions, the option counterparties and/or their respective affiliates expect to enter into various derivative transactions with respect to our common stock and/or purchase shares of our common stock concurrently with or shortly after the pricing of the notes. This activity could increase (or reduce the size of any decrease in) the market price of our common stock or the notes at that time. In addition, the option counterparties and/or their respective affiliates may modify their hedge positions by entering into or unwinding various derivatives with respect to our common stock and/or purchasing or selling our common stock or other securities of ours in secondary market transactions following the pricing of the notes and prior to the maturity of the notes (and are likely to do so during any observation period related to a conversion of notes). This activity could also cause or avoid an increase or a decrease in the market price of our common stock or the notes, which could affect your ability to convert the notes and, to the extent the activity occurs during any observation period related to a conversion of notes, it could affect the number of shares and value of the consideration that you will receive upon conversion of the notes.

For a discussion of the potential impact of any market or other activity by the option counterparties and/or their respective affiliates in connection with the capped call transactions, see **Risk Factors** **Risks Related to the Offering and the Notes** **The capped call transactions may affect the value of the notes and our common stock** and **Underwriting**.

NASDAQ Global Select Market Symbol for Our Common Stock

Our common stock is listed on The NASDAQ Global Select Market under the symbol ICPT.

Trustee, Paying Agent and Conversion Agent

U.S. Bank National Association.

Risk Factors

You should read the **Risk Factors** section of this prospectus supplement for a discussion of factors to consider carefully before deciding to purchase notes.

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Except as otherwise noted, we have presented the information in this prospectus supplement assuming:

no exercise by the underwriters in this offering of their over-allotment option; and
no exercise of outstanding stock options or vesting of outstanding restricted stock units.

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The following table sets forth summary consolidated financial data as of and for the periods presented. The summary consolidated financial data as of December 31, 2015 and 2014 and for the years ended December 31, 2015 and 2014 are derived from our audited condensed consolidated financial statements, which are incorporated by reference herein. The summary consolidated financial data as of March 31, 2016 and for the three months ended March 31, 2016 and 2015 are derived from our unaudited condensed consolidated financial statements, which are incorporated by reference herein. These unaudited condensed consolidated financial statements have been prepared on a basis consistent with our audited consolidated financial statements. The unaudited consolidated financial statements include all adjustments which we consider necessary for a fair presentation of the financial position and the results of operations for such periods.

Our historical results are not necessarily indicative of the results that may be expected in the future. The following summary consolidated financial data should be read in conjunction with the sections entitled **Risk Factors** and **Capitalization** in this prospectus supplement and our consolidated financial statements and the related notes thereto incorporated by reference herein.

	Years Ended December 31, 2015		Three Months Ended March 31, 2016	
	2014		2015	
	(in thousands, except per share data) (unaudited)			
Consolidated Statement of Operations Data:				
Licensing revenue	\$2,782	\$1,742	\$445	\$1,445
Costs and expenses:				
Research and development	128,193	80,311	37,413	27,966
General and administrative	103,745	34,601	90,432	13,138
Total costs and expenses	231,938	114,912	127,845	41,103
Other income (expense):				
Revaluation of warrants		(170,832)		
Other income, net	2,727	776	726	272
	2,727	(170,056)	726	272
Net loss	\$(226,429)	\$(283,226)	\$(126,674)	\$(39,386)
Net loss attributable to common stockholders	\$(226,429)	\$(283,226)	\$(126,674)	\$(39,386)
Net loss per share, basic and diluted	\$(9.56)	\$(13.63)	\$(5.17)	\$(1.78)
Weighted average shares outstanding, basic and diluted	23,694	20,784	24,495	22,172
		December 31, 2015	2014	March 31, 2016
		(in thousands)		(unaudited)
Consolidated Balance Sheet Data:				
Cash, cash equivalents and investment securities	\$ 628,055	\$ 239,724	\$ 556,860	
Working capital	594,320	230,587	475,695	

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Total assets	655,758	254,149	593,375
Long-term liabilities	6,236	8,017	5,790
Accumulated deficit	(695,630)	(469,202)	(822,305)
Total stockholders' equity	602,149	230,891	488,333

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RISK FACTORS

Investing in the notes involves significant risks. In deciding whether to invest, and in consultation with your own financial and legal advisors, you should carefully consider the risks and uncertainties described below, together with the other information contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein and any free writing prospectus that we may authorize for use in connection with this offering. Any of these risks could have a material adverse effect on our business, financial condition, results of operations and prospects and cause the value of our stock to decline, which could cause you to lose all or part of your investment. The risks and uncertainties we have described are not the only ones facing our company. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business operations.

Risks Related to Our Financial Position and Need for Additional Capital

We are dependent on the successful commercialization of Ocaliva™ (obeticholic acid), which received accelerated approval in May 2016 from the U.S. Food and Drug Administration, or FDA, as a treatment for primary biliary cholangitis, or 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 (obeticholic acid, or OCA) is our only drug that has been approved for sale and it has only been approved in the United States 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. We do not expect to generate significant sales revenues in 2016.

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.

While we have conducted pre-commercial activities, such as patient profiling, to better understand how physicians care for PBC patients, PBC is a rare disease in which no new therapy has been approved in approximately 20 years. 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 OCA 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 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 sustained revenues. It may take the passage of a significant amount of time to generate significant sustained revenues even if Ocaliva becomes accepted as a therapy in PBC. Furthermore, because Ocaliva is still undergoing regulatory review outside of the United States, we may not be able to commercialize Ocaliva in PBC outside of the United States, 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.

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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 \$126.7 million during the three months ended March 31, 2016 and net losses of \$226.4 million, \$283.2 million and \$67.8 million for the years ended December 31, 2015, 2014 and 2013, respectively. To date, we have financed our operations primarily through private placements of our convertible preferred stock, convertible notes and warrants to purchase common stock, public offerings of our common stock and payments received under our licensing and collaboration agreements with Sumitomo Dainippon Pharma Co., Ltd., or Sumitomo Dainippon, and Les Laboratoires Servier and Institut de Recherches Servier, which are collectively referred to as Servier. At March 31, 2016, we had \$556.9 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 the United States, seek regulatory approval for and prepare to commercially launch Ocaliva for PBC in other jurisdictions, develop and seek regulatory approvals for OCA in nonalcoholic steatohepatitis, or 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. 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 long-term safety extension phases of our clinical trials 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 continue our AESOP Phase 2 clinical trial of OCA for primary sclerosing cholangitis, or 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 trials, such as a Phase 2 clinical trial, referred to as the CONTROL trial, to assess the lipid metabolic effects of OCA and the effects of concomitant statin administration in NASH patients. Furthermore, in November 2015, we initiated a Phase 1 clinical trial for INT-767, an earlier stage product candidate. Our expenses could increase if we are required by the FDA or the European Medicines Agency, or 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 our product candidates 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 have never been profitable. We expect to incur losses for the foreseeable future, and we may never achieve or

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.

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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, including significant expenses relating to our sales, marketing and distribution capabilities and increasing our drug manufacturing activities. As part of our longer-term strategy, we also anticipate incurring significant expenses in connection with our planned increase in our product development, scientific, commercial and administrative personnel and expansion of our facilities and infrastructure in the United States and abroad. We expect to incur additional costs associated with operating as a public company and further plan on expanding our operations in the United States, Europe and in other countries such as Canada and Australia.

As of March 31, 2016, we had \$556.9 million in cash, cash equivalents and investment securities. We currently project adjusted operating expenses in the range of \$360 million to \$400 million in the fiscal year ending December 31, 2016, which excludes the \$45.0 million net expense for the settlement of the purported securities class action lawsuit, stock-based compensation and other non-cash items. These expenses are planned to support the commercialization of Ocaliva in PBC, continued clinical development for OCA in PBC, NASH and PSC, increased OCA manufacturing activities and the continued development of INT-767 and other pipeline programs. We completed the build out of our U.S. commercial infrastructure for the PBC commercial launch with the hiring of a number of senior leaders in our U.S. commercial organization throughout 2015, along with the hiring of our U.S. territory business managers and other field personnel in October 2015. We also significantly expanded our commercial and other infrastructure internationally in 2015. Furthermore, we have devoted significant resources to building a global medical affairs team over the course of 2015 to support appropriate disease state, medical and scientific interactions with the healthcare and scientific community. We plan on making additional investments over 2016 should key regulatory milestones be achieved on a timely basis. Accordingly, we will continue to require substantial additional capital in connection with our continuing operations, including continuing our clinical development and commercialization activities. Because successful development of our product candidates is uncertain, we are unable to estimate the actual funds required to complete the research and development and commercialization of our products under development.

Adjusted operating expense is a financial measure not calculated in accordance with U.S. generally accepted accounting principles, or GAAP. Other than the \$45 million net expense for the settlement of the purported class action lawsuit, 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. See 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 prospectus supplement, and our rapid growth and expansion, we currently cannot accurately or precisely predict the duration beyond 2017 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 commercialization of Ocaliva for PBC in the United States at least through the end of 2017; prepare for and, if we obtain marketing approval on a timely basis, initiate the commercial launch of Ocaliva in PBC in certain European countries as well as other target markets across the world such as Canada and Australia, but not commercially launch Ocaliva in PBC in other countries across the world; continue and expand our clinical development programs for OCA in PBC, NASH and PSC, such as continuing, but not completing, our planned Phase 3 clinical program for OCA in NASH, including the REGENERATE trial, our ongoing AESOP trial for OCA in PSC, and our ongoing COBALT confirmatory clinical outcomes trial of OCA in PBC; and

We will require substantial additional funding, which may not be available to us on acceptable terms, or at all, and, i

advance the continued development of INT-767, including the completion of the ongoing Phase 1 clinical trial, and our preclinical compounds, but not completing the clinical or preclinical development needed, as the case may be, for INT-767 or our preclinical compounds.

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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 the United States; our ability to receive marketing approval of Ocaliva for PBC in Europe based on our regulatory submissions package and our work completed to date, including the willingness of the EMA 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 outside of the United States if we receive marketing authorization;

the progress, costs, results of and timing of our clinical development programs for OCA in PBC, NASH and other indications, such as the sufficiency of the REGENERATE trial to be accepted as the sole pivotal trial for marketing approval or the acceptability of a surrogate endpoint for accelerated approval of OCA for the treatment of NASH and any modifications we may be required to make to the COBALT trial as part of our post-marketing requirements to the FDA;

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 which is in a Phase 1 clinical trial, and our product candidates in preclinical development such as INT-777; the significant 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 product candidates;

market acceptance of our product candidates, which may be affected by the reimbursement that our products receive 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.

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The terms of any financing may adversely affect the holdings or the rights of our securityholders. 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, 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 have not yet received marketing approval for Ocaliva in PBC in the European Union and we do not have approval for any of our other product candidates. We currently do not know when we will be able to start realizing sales revenue and do not expect to generate significant sales revenue in 2016.

While we commercially launched Ocaliva for PBC in the United States, we will need to conduct further activities to develop and cultivate a sustainable market for our drug in this rare 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;
- 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;

We have a limited operating history as a commercial organization, which may make it difficult to predict our future p

our ability to establish and maintain an effective sales and marketing infrastructure directly or through collaborations with third parties;

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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 Product Candidates

We cannot be certain if Ocaliva will receive full approval in the United States for PBC or that Ocaliva will be approved for PBC outside of the United States. 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 a New Drug Application, or NDA, from the FDA or a Marketing Authorization Application, or 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 and it has only been approved in the United States for the treatment of 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, we are discussing modifications to the COBALT trial to potentially include a broader cross-section of PBC patients with early, moderately advanced and advanced disease according to the so-called Rotterdam criteria. 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.

In Europe, we completed the submission of our MAA for Ocaliva in PBC in June 2015. If we are successful in the EMA review process, we anticipate receiving marketing approval for PBC in late 2016, with planned commercial launches thereafter in certain European countries leading to anticipated revenues in 2017.

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We also plan to apply for marketing approval of Ocaliva for PBC in other markets across the world such as Australia and Canada. As part of the regulatory review process of Ocaliva for PBC, the EMA will continue to review our submission package and conduct regulatory inspections of us and our vendors. We have provided responses as to many of the issues that have been identified in the regulatory review process and continue to respond with respect to others. We may be requested to provide further information, which may impact our regulatory review process. It remains possible that one or more of the issues identified to date, or other issues that may be identified by the EMA as the review process continues, may result in the EMA not approving our marketing application or delaying approval. As a result, we cannot be certain that our application will be reviewed in a timely manner or approved by the EMA.

We currently have no other products approved for sale and we cannot guarantee that we will ever have additional marketable products.

NDA's and MAA's must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety and effectiveness for each desired indication. NDA's and MAA's 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, on June 23, 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 the approval of our 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 the 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 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.

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 initiated our Phase 3 REGENERATE trial of OCA in non-cirrhotic NASH patients with liver fibrosis in September 2015 and initiated our Phase 2 CONTROL trial to characterize the lipid metabolic effects of OCA and cholesterol management effects of concomitant statin administration in NASH patients in December 2015. We also intend to complete our planning for a Phase 2 program in NASH patients with cirrhosis in 2016. In each of these cases, our ability to obtain the approvals necessary to commercialize our product candidates will depend on our ability to conduct and complete these additional trials as well as assemble various other

We cannot be certain if Ocaliva will receive full approval in the United States for PBC or that Ocaliva will be approved

data to complete our regulatory filings for OCA in the relevant indication or patient population.

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There can be no assurance that we will be able to receive marketing approval for OCA in PBC outside of the United States or 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 histological endpoint is similar to that in the Phase 2b clinical trial for the treatment of NASH, known as the FLINT trial, sponsored by the U.S. National Institute of Diabetes and Digestive and Kidney Diseases, or NIDDK, a part of the National Institutes of Health, our Phase 3 REGENERATE trial has different trial designs. For example, the REGENERATE trial will include the following interim co-primary endpoints which are intended to serve as the basis for seeking marketing approvals in the United States, Europe and other countries: (i) the proportion of OCA-treated patients relative to placebo achieving at least one stage of liver fibrosis improvement with no worsening NASH and (ii) the proportion of OCA-treated patients relative to placebo achieving NASH resolution with no worsening of liver fibrosis. 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 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 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. Although Sumitomo Dainippon has informed us that it is exploring the initiation of a Phase 3 clinical trial for OCA in NASH patients intended to support the registration of this indication in Japan, the results may not be an improvement as compared to those from the Phase 2 trial on Japanese NASH patients and there is no assurance that Sumitomo Dainippon will initiate a Phase 3 clinical trial.

If we are unable to obtain approval from the FDA, the EMA or other regulatory agencies for OCA and our other product candidates, or if, subsequent to approval, we are unable to successfully commercialize OCA or our other product candidates, 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

We are developing product candidates for the treatment of rare diseases or diseases for which there are ~~15~~ or limited

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. Under Subpart H regulations, the FDA can grant accelerated approval based on a surrogate reasonably likely to predict clinical benefit. Even if results from our planned pivotal clinical trials for a specific indication are highly

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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. If a confirmatory clinical outcomes trial is required, 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 the FDA, we initiated our COBALT clinical outcomes confirmatory trial in PBC in December 2014 prior to the approval of Ocaliva. We are currently discussing modifications to the COBALT trial to potentially include a broader cross-section of PBC patients with early, moderately advanced and advanced disease according to the so-called Rotterdam criteria to evaluate the safety and efficacy of Ocaliva as a monotherapy in patients with PBC. There can be no assurance that our COBALT trial will confirm that the surrogate endpoints used for accelerated approval will eventually show an adequate correlation with clinical outcomes. If the COBALT trial fails to show such adequate correlation, we may not be able to maintain our previously granted marketing approval for Ocaliva in PBC.

Likewise, while we completed our filing of the MAA with the EMA in June 2015, we will not receive definitive feedback from the EMA prior to formal review of our MAA as to the acceptability of the POISE trial endpoint to support a marketing authorization of Ocaliva for the treatment of PBC. In order to support the clinical utility of the surrogate endpoint for Ocaliva as a treatment for PBC, we have sponsored an independent study pooling and analyzing long-term PBC patient data from a number of leading PBC academic centers, which we refer to as the Global PBC Study Group. Furthermore, an academic consortium in the United Kingdom has published the results of another large observational study in PBC patients in the United Kingdom. Although we believe the results of both studies are supportive of the clinical utility of our surrogate endpoint for the use of Ocaliva in PBC, the supporting data may still not be accepted by the EMA in its consideration of the adequacy of our surrogate endpoint under an MAA for Ocaliva for the treatment of PBC. In addition to the risk around the acceptability of the surrogate biochemical endpoint to support accelerated approval, there are quality assurance risks around the data supporting assessment of the biochemical endpoint. It is possible that key parameters such as the validation of the assay and consistency across laboratories will not be acceptable to EMA and could delay or jeopardize marketing approval by the EMA.

It is also possible that any marketing authorization we receive from the EMA for Ocaliva for the treatment of PBC could be conditional on post-approval studies and not considered a full approval. 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 a clinical outcomes trial 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

We are developing product candidates for the treatment of rare diseases or diseases for which there are ~~17~~ or limited

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.

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Our Phase 3 REGENERATE trial of OCA in non-cirrhotic NASH patients with liver fibrosis, which was initiated in September 2015, incorporates interim co-primary surrogate endpoints 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 NAFLD activity score (a system of scoring the histopathological features in the liver), or NAS, with no worsening of liver fibrosis and the co-primary endpoints for our REGENERATE trial are: (i) the proportion of OCA-treated patients relative to placebo achieving at least one stage of liver fibrosis improvement with no worsening NASH and (ii) the proportion of OCA-treated patients relative to placebo achieving NASH resolution with no worsening of liver fibrosis. 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. 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.

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 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 initiated our Phase 4 COBALT clinical outcomes confirmatory trial of OCA in PBC in December 2014, our Phase 2 AESOP trial of OCA in PSC in December 2014, our Phase 3 REGENERATE trial of OCA in NASH in September 2015, our Phase 2 CARE trial of OCA in biliary atresia in October 2015 and our Phase 2 CONTROL trial to assess the lipid metabolic effects of OCA and the effects of concomitant statin administration in NASH patients in December 2015. The results from these trials may not be

Delays in the commencement, enrollment and completion of clinical trials could result in increased costs to us and

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 of our other product candidates will begin on time or will be completed on schedule, if at all.

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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 institutional review boards, or 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 and Servier 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 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 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.

Changes in regulatory requirements and guidance may also occur and we or any of our collaborators may need to amend clinical trial protocols to reflect these changes with appropriate regulatory authorities. Amendments may require us or any of our collaborators to resubmit clinical trial protocols to IRBs for re-examination, which may impact the costs, timing or successful completion of a clinical trial.

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, Servier 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

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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 for PBC, its full approval depends on the results of the Phase 4 COBALT confirmatory outcomes trial. We cannot assure you that the COBALT trial 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 farnesoid X receptor, or FXR. With the exception of the endogenous human bile acid chenodeoxycholic acid, or 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

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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 Phase 2 PBC clinical trial of OCA in combination with ursodiol, approximately 8% of the patients enrolled in the 10 mg and 25 mg dose groups withdrew from the trial due to severe pruritus. At the 50 mg dose, approximately 25% of the patients withdrew from the trial due to severe pruritus. 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.

Ocaliva is contraindicated for patients with complete biliary obstruction. For patients with moderate or severe hepatic impairment, which represents approximately 3% of PBC patients, the U.S. label for Ocaliva in PBC includes an adjustment in the 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.

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. In December 2015, we initiated CONTROL, a Phase 2 trial characterizing the lipid metabolic effects of OCA and cholesterol management effects of concomitant statin administration in NASH patients. There were two patient deaths in the FLINT trial, and neither death was considered related to OCA treatment.

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

Our product candidates may have undesirable side effects which may delay or prevent marketing approval, or, if approved,

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. It is also possible that patients receiving treatment from OCA or our drug candidates for the labeled indication may suffer from other concomitant illnesses that may increase the likelihood of certain adverse events. It may be difficult to discern

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whether certain events or symptoms observed during our trials were due to our drug candidates or placebo, 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 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, which could delay or preclude regulatory approval of OCA or limit its commercial use.

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

regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies;

we may be required to change instructions regarding the way the product is administered, conduct additional clinical trials or change the labeling of the product;

we may be subject to limitations on how we may promote the product;
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.

Any of these events could prevent us, Sumitomo Dainippon, Servier or our potential future collaborators from achieving or maintaining market acceptance of the affected product or could substantially increase commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenues from the sale of our products.

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

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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 drug designation in Europe will not be maintained following approval if the EMA determines that the product does not satisfy the requisite criteria including demonstration of significant clinical benefit. In November 2015, the European Commission set forth a consultation document and a notice detailing proposed amendments to the rules governing orphan medicinal products which may make it more difficult to demonstrate significant clinical benefit at the time of marketing authorization. The result of this process may impact our ability to maintain orphan drug designation in Europe.

The failure to maintain orphan status may impact our ability to receive a premium price for OCA or our other products and 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 the later 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.

If the FDA and EMA and other regulatory agencies do not approve the manufacturing facilities of our future contract manufacturers for commercial production on a timely basis or at all, we may not be able to commercialize any of our product candidates or commercialization of our product candidates could be delayed.

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 the COBALT clinical outcomes confirmatory trial of OCA in PBC and the long-term safety extension phase of the POISE trial for OCA in PBC, our Phase 3 NASH program for OCA, including the REGENERATE trial, and the certain other 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.

While we have procured sufficient supplies for the commercial launch of Ocaliva in PBC, we may not be able to reach agreements with these or other contract manufacturers for sufficient supplies to continue commercial sales on a long-term basis. We do not have agreements for commercial supplies of OCA or any of our other product candidates. We currently obtain these supplies and services from our third-party contract manufacturers on a purchase order basis. We are currently seeking to qualify one or more back-up API manufacturers.

If the FDA and EMA and other regulatory agencies do not approve the manufacturing facilities of our future contract

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 product candidates will not be approved or, if already approved, may be subject to recalls.

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

the possibility that we are unable to enter into 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 commercialization of our product candidates, cause us to incur higher costs, prevent us from commercializing our 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 for our product candidates and to have any such new source approved by the government agencies that regulate our products.

Even if our product candidates receive regulatory approval, we will still be subject to strict regulatory requirements governing manufacturing and marketing of our products and, as a result, we could face future development and regulatory difficulties.

Our product candidates, if approved, will also be subject to ongoing regulatory requirements for labeling, packaging, storage, advertising, promotion, record-keeping and submission of safety and other post-market information. In addition, approved products, manufacturers and 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 Good Manufacturing Practices, or 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 will also be 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 our approved products for indications or uses for which they are not 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 warning letters;

mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;

Even if our product candidates receive regulatory approval, we will still be subject to strict regulatory requirements g

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;

impose other administrative or judicial civil or criminal penalties;

withdraw regulatory approval;

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refuse to approve pending applications or supplements to approved applications filed by us, Sumitomo Dainippon, Servier or our potential future collaborators;

impose restrictions on operations, including costly new manufacturing requirements; or
seize or detain products.

Risks Related to the Commercialization of Our Products

Reimbursement decisions by third-party payors may have an adverse effect on pricing and market acceptance of Ocaliva or our product candidates, if approved. If there is not sufficient reimbursement for our products or they are not covered at all, it is less likely that they will be widely used.

Market acceptance and sales of any products or product candidates that we develop will depend on reimbursement policies and may be affected by future healthcare reform measures. 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. We cannot be certain that reimbursement will be available for Ocaliva or any other products and product candidates that we develop. Also, reimbursement policies could reduce the demand for, or the price paid for, our products. 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 the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or 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. The goal of 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.

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 recently commenced the launch of Ocaliva for PBC in the United States with a monthly list price of \$5,700. We do not know if the price we have selected for Ocaliva will receive broad acceptance from

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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.

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, and in some countries we expect that it may exceed 12 months. Even after a price is negotiated, countries frequently request or require adjustments to the price and other concessions over time. 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.

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.

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. For PBC, the current standard of care is ursodiol. 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. 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;

Ocaliva and other product candidates, if approved, may not achieve broad market acceptance among physicians, p

timing of market introduction and perceived effectiveness of competitive products;
the degree of cost-effectiveness;

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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 upper limit of normal, or 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 or distribution experience as a commercial organization. The commercial launch of Ocaliva for PBC in the United States represents our first product launch. We also plan to commercialize Ocaliva for PBC in Europe, Canada and certain other countries 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.

We have limited sales, marketing or distribution experience and we will have to invest in significant additional resources.

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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 Japan, China, South Korea and potentially other Asian countries, if approved, and a collaboration with Servier to assist in the development and commercialization of certain of our earlier stage agonists of a dedicated bile acid receptor called TGR5 outside of the United States and Japan, if approved, and may elect to seek additional strategic collaborators for our product candidates. 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.

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 prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, or causing to be made, a false statement to get a false claim paid. The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service 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. Most states also have statutes or regulations similar to the federal anti-kickback law and federal false claims laws, which apply to items and services covered by Medicaid and other state programs, or, in several states, apply regardless of the payor. Administrative, civil and criminal sanctions may be imposed under these federal and state laws.

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.

If we market products in a manner that violates healthcare fraud and abuse laws, or if we violate government price

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

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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 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 strategic collaborations in place relating to certain of our product candidates. We entered into an exclusive license agreement with Sumitomo Dainippon regarding the development and commercialization of Ocaliva for PBC and OCA for NASH in Japan, China and South Korea and provided Sumitomo Dainippon with an option to extend its exclusive license to different indications as well as certain other Asian countries. We entered into a strategic collaboration with Servier initially focused on the identification and optimization of novel TGR5 agonists for the treatment of type 2 diabetes and other associated disorders. Although our licensing and collaboration agreement with Servier expired in September 2015, we have continued our collaborative relationship with Servier while we negotiate a new agreement. These strategic collaborations may not be scientifically or commercially successful due to a number of important factors, including the following:

Sumitomo Dainippon and Servier have significant discretion in determining the efforts and resources that each will apply to their strategic collaboration with us. The timing and amount of any cash payments, milestones and royalties that we may receive under such agreements will depend on, among other things, the efforts, allocation of resources and successful development and commercialization of our product candidates by Sumitomo Dainippon and Servier under their respective agreements;

Our agreement with Servier provides it with wide discretion in deciding which novel compounds to advance through the preclinical and clinical development process. It is possible for Servier to reject certain compounds at any point in the research, development and clinical trial process without triggering a termination of their agreement with us;

If any of our current strategic collaborators fails to perform its obligations or terminates its agreement with us, the de

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 and our agreement with Servier restricts it from developing or commercializing any TGR5 receptor agonist during the term of the agreement other than pursuant to

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the Servier agreement. Subject to these restrictions, it is possible that Sumitomo Dainippon or Servier 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 they license from us;

Sumitomo Dainippon or Servier may change the focus of their development and commercialization efforts or pursue higher-priority programs;

Sumitomo Dainippon or Servier may, under specified circumstances, terminate their strategic collaborations 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 and Servier have, 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 collaborators do not, our ability to do so may be compromised by our strategic collaborators' acts or omissions;

Sumitomo Dainippon or Servier 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 or Servier may not comply with all applicable regulatory requirements, or fail to report safety data in accordance with all applicable regulatory requirements.

If either Sumitomo Dainippon or Servier fails to develop or effectively commercialize OCA or any TGR5 compounds, respectively, we may not be able to replace them with another collaborator. For example, although Sumitomo Dainippon has informed us that it is exploring the initiation of a Phase 3 clinical trial for OCA in NASH patients intended to support the registration of this indication in Japan, Sumitomo Dainippon may ultimately decide not to pursue such a trial or cease continuing development despite commencing the trial. 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 not be successful in establishing 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 collaborations with Sumitomo Dainippon for OCA and Servier for our earlier stage TGR5 program. We may establish additional collaborations for development and commercialization of OCA in territories outside of those licensed by Sumitomo Dainippon or for our earlier stage TGR5 program in the United States or Japan and for other product candidates and research programs, including INT-767 and 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.

We may not be successful in establishing and maintaining development and commercialization collaborations, which

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 Japan, China and

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South Korea and a right of first refusal to license OCA in several other Asian countries. 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 collaborations with Sumitomo Dainippon and Servier, 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 for the second line treatment of PBC. Among our other product candidates, only INT-767, which is undergoing Phase 1 clinical trials, is currently in clinical development. One of our strategies is to pursue clinical development of OCA for other orphan and more common indications, to the extent that we have sufficient funding.

PBC is a rare 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, 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 face competition from other biotechnology and pharmaceutical companies and 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

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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 Albireo AB, Akarna Therapeutics Ltd., AstraZeneca plc, Biotie Therapies Corp. (acquired by Acorda Therapeutics, Inc.), Boehringer Ingelheim GmbH, Bristol-Myers Squibb Company, Conatus Pharmaceuticals Inc., Dr. Falk Pharma GmbH, Durect Corporation, Eli Lilly, Enanta Pharmaceuticals, Inc., ENYO Pharma SAS, Exelixis, Inc., FibroGen, Inc., FF Pharmaceuticals BV, Galectin Therapeutics Inc., Galmed Medical Research Ltd., Genfit SA, Genkyotex SA, Gilead Sciences, Inc., GlaxoSmithKline, Immuron Ltd., Islet Sciences, Inc., Medivation, Inc., MiNA Therapeutics, NGM Biopharmaceuticals, Nitto Denko Corporation, Novartis International AG, Novo Nordisk A/S, NuSirt Biopharma, Inc., Protalix Biotherapeutics, Shire plc, Tobira Therapeutics, Inc., Viking Therapeutics, Inc. and Zydus Pharmaceuticals Inc. Ongoing Phase 3 clinical trials for the treatment of PBC include an investigator-sponsored trial of bezafibrate, a fibrate that has not been approved for commercialization by the FDA and is only available outside of the United States, and a combination of ursodiol and budesonide, a steroid, sponsored by Dr. Falk Pharma GmbH. 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 2 clinical trials in NASH patients of various disease severity with both simtuzimab, an anti-body against the lysyl oxidase-like 2 enzyme, and GS-4997, an inhibitor of the apoptosis signal-regulating kinase 1. Gilead Sciences, Inc. is also studying an FXR agonist (GS-9674) for the treatment of NASH. A number of 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 FDA approval of Ocaliva in 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 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 (such as metformin), antihyperlipidemic agents (such as 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;

We face competition from other biotechnology and pharmaceutical companies and our operating results will suffer if

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;

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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.

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 in the United States 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. 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. Several years ago, 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

We depend on third-party contractors for a substantial portion of our operations and may not be able to control their

of clinical trials violates applicable law.

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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.

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 also currently have an Italian subsidiary that acts as our legal representative for our clinical trials in the European Union to satisfy European Union regulatory requirements. 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. In addition, we have entered into collaborations with Sumitomo Dainippon for the development of OCA and Servier for our earlier stage TGR5 program, 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, including:

- differing regulatory requirements for drug approvals internationally;
- 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;
- 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; and
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters, including earthquakes, volcanoes, typhoons, floods, hurricanes and fires.

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.

A variety of risks associated with our international business operations and our planned international business relat

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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. 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 NASH program. We may experience difficulties in managing our significant growth.

From December 31, 2014 to March 31, 2016, our employee base has grown from 136 to 424 employees. Of the 424 employees as of March 31, 2016, 194 employees were in our drug development operations, 146 employees were in our commercial group and 84 employees were in our corporate group. At March 31, 2016, 318 employees were based in the United States, 99 employees were based in Europe and 7 employees were based in Canada. 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, both for our ongoing pre-commercial activities and for the launch and ongoing marketing and sale of any product candidate for which we obtain marketing approval. 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, including our wholly-owned subsidiary in the United Kingdom. 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, Canada and Australia, 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 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

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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; David Shapiro, our chief medical 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.

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

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

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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 a product candidate and may have to limit its commercialization.

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 for 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 \$10 million. We have clinical trial 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.

We face potential product liability exposure, and if successful claims are brought against us, we may incur substantial

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

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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 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 acquiring businesses, technologies or products 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 businesses, technologies and products;
- 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 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.

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. 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 Health Insurance Portability and Accountability Act, or HIPAA, and its implementing regulations impose, among other requirements,

If we engage in an acquisition, reorganization or business combination, we will incur a variety of risks that could adversely

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. We have in the past relied on adherence to the U.S.-EU Safe Harbor Framework as agreed to and set forth by the U.S. Department of

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Commerce and the European Commission as a means to legitimize certain transfers of personal information from the European Economic Area, or EEA, to the United States. However, a recent opinion of the European Union Court of Justice, or ECJ, deemed the U.S.-EU Safe Harbor Framework an invalid method of protecting the transfer of personal information from the EEA to the United States. While we are engaging in efforts to address the implications of the ECJ opinion and actively employing other means to legitimize the transfer of personal information from the EEA to the United States, we may be unsuccessful in these efforts. Failure to comply with laws regarding data protection could expose us to risk of enforcement actions and the potential for significant penalties as well as the loss of access to certain data from the EU. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and can generate negative publicity, which could harm our business.

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 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 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 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, identical or competitive to ours or important to our business. We cannot be certain that any patent application owned by a third party will not have priority over patent applications filed or in-licensed by us, or that we or our licensors will not be involved in interference, derivation, opposition or invalidity proceedings before U.S. or non-U.S. patent offices.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

others may be able to 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 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.

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As of March 31, 2016, 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 71 pending U.S. and non-U.S. patent applications relating to OCA in these areas.

In addition, as of March 31, 2016, we were the owner of record of over 160 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 95 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 product candidates, our ability to assert our patents to stop others from using or selling our product candidates in a non-pharmaceutically acceptable formulation 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 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 product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of OCA and our other product candidates, if any, one or more of our 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

If we do not obtain protection under the Hatch-Waxman Act and similar legislation outside of the United States by e

during product development and the FDA regulatory review process. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, 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 anticipate applying for an extension to the patent term for this

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patent in the United States through 2027. We expect to take similar actions in other 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.

If we choose to go to court 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 to rule that such patents are invalid, not infringed, or should not be enforced against that third party. These lawsuits 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 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 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 recently modified some tests used by the U.S. Patent and Trademark Office, or 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 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 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 product candidates to market and be precluded from manufacturing or selling our product candidates.

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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 an outside firm and rely on our outside counsel to pay these fees due to 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

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may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all. 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. We have approximately 50 trademark and service mark registrations and approximately 272 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.

In addition, we have not yet received final approval from regulatory authorities for a proprietary name for any of our product candidates, including OCA, in any jurisdiction. Any proprietary name we propose to use with OCA in the United States and Europe must be approved by the FDA and EMA, respectively, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA and EMA typically conduct a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA or EMA objects to our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable proprietary product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the regulatory agencies.

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

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Risks Related to the Offering and the Notes

We may invest or spend the proceeds of this offering in ways with which you may not agree or in ways which may not yield a significant return, if any.

We will have broad discretion over the use of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of this offering and/or for purposes that do not obtain a significant return, if any, on investment. You may not agree with the manner in which we choose to allocate and spend these net proceeds and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not increase our operating results or market value. Until the net proceeds are used, they may be placed in investments that do not produce significant income or investments that lose value.

The notes will be effectively subordinated to any future secured debt we may incur and to any liabilities of our subsidiaries.

The notes will rank senior in right of payment to our future indebtedness that is expressly subordinated in right of payment to the 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) of our subsidiaries.

In the event of our bankruptcy, liquidation, reorganization or other winding up, our assets that secure debt ranking senior in right of payment to the notes will be available to pay obligations on the notes only after such secured debt has been repaid in full from these assets. There may not be sufficient assets remaining to pay amounts due on any or all of the notes then outstanding. The indenture governing the notes does not prohibit us from incurring additional senior debt or secured debt, nor does it prohibit any of our subsidiaries from incurring additional liabilities.

As of March 31, 2016, we had no outstanding consolidated indebtedness and total consolidated liabilities of \$105.0 million, \$4.8 million of which were owed by our subsidiaries (including trade payables), to which the notes would have been structurally subordinated. After giving effect to the issuance of the notes (assuming no exercise of the underwriters' over-allotment option), our total consolidated indebtedness and other liabilities would have been \$505.0 million as of March 31, 2016.

The notes will be our obligations only and will not be guaranteed by any of our subsidiaries.

The notes will be our obligations exclusively and will not be guaranteed by any of our subsidiaries. Our right to receive assets from any of our subsidiaries upon their respective liquidations or reorganizations, and the right of holders of the notes to participate in those assets, is structurally subordinated to claims of each such subsidiary's creditors, including trade creditors. Even if we were a creditor of any of our subsidiaries, our rights as a creditor would be subordinate to any security interest in the assets of that subsidiary and any indebtedness of that subsidiary senior to that held by us. Our subsidiaries are separate and distinct legal entities and have no obligation, contingent or otherwise, to make payments under the notes or to make any funds available for that purpose. In addition, dividends, loans or other distributions to us from such subsidiaries may be subject to contractual and other restrictions or subject

to other business considerations. For these reasons, we may not have access to sufficient assets or cash flows of our subsidiaries to make required payments under the notes.

Servicing the notes will require a significant amount of cash, and we may not have sufficient cash flow from our business to make payments under the notes.

Our ability to make scheduled payments of the principal of, to pay interest on or to refinance the 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 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

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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 not have the ability to raise the funds necessary to settle conversions of the notes or to repurchase the notes upon a fundamental change, and our future debt may contain limitations on our ability to pay cash upon conversion or repurchase of the notes.

Holders of the notes will have the right to require us to repurchase their notes upon the occurrence of a fundamental change at a fundamental change repurchase price equal to 100% of the principal amount of the notes to be repurchased, *plus* accrued and unpaid interest, if any, as described under Description of Notes Fundamental Change Permits Holders to Require Us to Repurchase Notes. In addition, upon conversion of the notes, unless we elect to deliver solely shares of our common stock to settle such conversion (other than paying cash in lieu of delivering any fractional share), we will be required to make cash payments in respect of the notes being converted as described under Description of Notes Conversion Rights Settlement upon Conversion. However, we may not have enough available cash or be able to obtain financing at the time we are required to make repurchases of notes surrendered therefor or notes being converted. In addition, our ability to repurchase the notes or to pay cash upon conversions of the notes may be limited by law, by regulatory authority or by agreements governing our future indebtedness. Our failure to repurchase notes at a time when the repurchase is required by the indenture or to pay any cash payable on future conversions of the notes as required by the indenture would constitute a default under the indenture. A default under the indenture or the fundamental change itself could also lead to a default under agreements governing our future indebtedness. If the repayment of the related indebtedness were to be accelerated after any applicable notice or grace periods, we may not have sufficient funds to repay the indebtedness and repurchase the notes or make cash payments upon conversions thereof.

Recent and future regulatory actions and other events may adversely affect the trading price and liquidity of the notes.

We expect that many investors in, and potential purchasers of, the notes will employ, or seek to employ, a convertible arbitrage strategy with respect to the notes. Investors that employ a convertible arbitrage strategy with respect to convertible debt instruments typically implement that strategy by selling short the common stock underlying the convertible notes and dynamically adjusting their short position while they hold the notes. Investors may also implement this strategy by entering into swaps on our common stock in lieu of or in addition to short selling the common stock. As a result, any specific rules regulating equity swaps or short selling of securities or other governmental action that interferes with the ability of market participants to effect short sales or equity swaps with respect to our common stock could adversely affect the ability of investors in, or potential purchasers of, the notes to conduct the convertible arbitrage strategy that we believe they will employ, or seek to employ, with respect to the notes. This could, in turn, adversely affect the trading price and liquidity of the notes.

The SEC and other regulatory and self-regulatory authorities have implemented various rules and taken certain actions, and may in the future adopt additional rules and take other actions, that may impact those engaging in short selling activity involving equity securities (including our common stock). Such rules and actions include Rule 201 of SEC Regulation SHO, the adoption by the Financial Industry Regulatory Authority, Inc. and the national securities exchanges of a Limit Up-Limit Down program, the imposition of market-wide circuit breakers that halt trading of securities for certain periods following specific market declines, and the implementation of certain regulatory reforms

Servicing the notes will require a significant amount of cash, and we may not have sufficient cash flow from our busi

required by the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, or Dodd-Frank. Any governmental or regulatory action that restricts the ability of investors in, or potential purchasers of, the notes to effect short sales of our common stock, borrow our common stock or enter into swaps on our common stock could adversely affect the trading price and the liquidity of the notes. In addition, Dodd-Frank and implementing regulations prohibit banking entities and their affiliates from engaging in proprietary trading in financial instruments, or the so-called Volcker Rule. These restrictions will limit the ability of banking entities and their affiliates to invest in or purchase the notes and could, in turn, adversely affect the trading price and liquidity of the notes.

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Volatility in the market price and trading volume of our common stock could adversely impact the trading price of the notes.

The stock market in recent years has experienced significant price and volume fluctuations that have often been unrelated to the operating performance of companies. In addition, 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. A decrease in the market price of our common stock would likely adversely impact the trading price of the notes. The market price of our common stock could also be affected by possible sales of our common stock by investors who view the notes as a more attractive means of equity participation in us and by hedging or arbitrage trading activity that we expect to develop involving our common stock. This trading activity could, in turn, affect the trading price of the notes. See Risk Factors Risks Related to Ownership of our Common Stock Our stock price has been and may in the future be volatile, which could cause holders of our common stock and the notes to incur substantial losses.

We may incur substantially more debt or take other actions which would intensify the risks discussed above.

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 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 notes that could have the effect of diminishing our ability to make payments on the notes when due.

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

In the event the conditional conversion feature of the notes is triggered, holders of notes will be entitled to convert the notes at any time during specified periods at their option. See Description of Notes Conversion Rights. If one or more holders elect to convert their 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 notes, we could be required under applicable accounting rules to reclassify all or a portion of the outstanding principal of the 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 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 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 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 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 notes to their face amount over the term of the 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 notes.

In addition, under certain circumstances, convertible debt instruments (such as the 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 notes will not be included in the calculation of

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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 notes, then our diluted earnings per share would be adversely affected.

Holders of notes will not be entitled to any rights with respect to our common stock, but they will be subject to all changes made with respect to them to the extent our conversion obligation includes shares of our common stock.

Holders of notes will not be entitled to any rights with respect to our common stock (including, without limitation, voting rights and rights to receive any dividends or other distributions on our common stock) prior to the conversion date relating to such notes (if we have elected to settle the relevant conversion by delivering solely shares of our common stock (other than paying cash in lieu of delivering any fractional share)) or the last trading day of the relevant observation period (if we elect to pay and deliver, as the case may be, a combination of cash and shares of our common stock in respect of the relevant conversion), but holders of notes will be subject to all changes affecting our common stock. For example, if an amendment is proposed to our certificate of incorporation or bylaws requiring stockholder approval and the record date for determining the stockholders of record entitled to vote on the amendment occurs prior to the conversion date related to a holder's conversion of its notes (if we have elected to settle the relevant conversion by delivering solely shares of our common stock (other than paying cash in lieu of delivering any fractional share)) or the last trading day of the relevant observation period (if we elect to pay and deliver, as the case may be, a combination of cash and shares of our common stock in respect of the relevant conversion), such holder will not be entitled to vote on the amendment, although such holder will nevertheless be subject to any changes affecting our common stock.

The conditional conversion feature of the notes could result in your receiving less than the value of our common stock into which the notes would otherwise be convertible.

Prior to the close of business on the business day immediately preceding January 1, 2023, you may convert your notes only if specified conditions are met. If the specific conditions for conversion are not met, you will not be able to convert your notes, and you may not be able to receive the value of the cash, common stock (and cash in lieu of any fractional shares) or a combination of cash and common stock, as applicable, into which the notes would otherwise be convertible.

Upon conversion of the notes, you may receive less valuable consideration than expected because the value of our common stock may decline after you exercise your conversion right but before we settle our conversion obligation.

Under the notes, a converting holder will be exposed to fluctuations in the value of our common stock during the period from the date such holder surrenders notes for conversion until the date we settle our conversion obligation.

Upon conversion of the notes, we have the option to 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. If we elect

Holders of notes will not be entitled to any rights with respect to our common stock, but they will be subject to all changes

to satisfy our conversion obligation in cash or a combination of cash and shares of our common stock, the amount of consideration that you will receive upon conversion of your notes will be determined by reference to the volume-weighted average price of our common stock for each trading day in a 20 trading day observation period. As described under Description of Notes Settlement upon Conversion, this period would be (i) if the relevant conversion date occurs prior to January 1, 2023 and we have not issued a notice of redemption with respect to the notes as described under Description of Notes Optional Redemption, the 20 consecutive trading days beginning on, and including, the second trading day immediately succeeding such conversion date; (ii) if the relevant conversion date occurs on or after January 1, 2023 and we have not issued a notice of redemption with respect to the notes as described under Description of Notes Optional Redemption, the 20 consecutive trading days beginning on, and including, the

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22nd scheduled trading day immediately preceding the maturity date; and (iii) if the relevant conversion date occurs on or after the date of our issuance of a notice of redemption with respect to the notes as described under Description of Notes Optional Redemption and prior to the relevant redemption date (even if the relevant conversion date occurs on or after January 1, 2023), the 20 consecutive trading days beginning on, and including, the 22nd scheduled trading day immediately preceding such redemption date. Accordingly, if the price of our common stock decreases during this period, the amount and/or value of consideration you receive will be adversely affected. In addition, if the market price of our common stock at the end of such period is below the average volume-weighted average price of our common stock during such period, the value of any shares of our common stock that you will receive in satisfaction of our conversion obligation will be less than the value used to determine the number of shares that you will receive.

If we elect to satisfy our conversion obligation solely in shares of our common stock upon conversion of the notes, we will be required to deliver the shares of our common stock, together with cash for any fractional share, on the third business day following the relevant conversion date. Accordingly, if the price of our common stock decreases during this period, the value of the shares that you receive will be adversely affected and would be less than the conversion value of the notes on the conversion date.

The notes will not be protected by restrictive covenants.

The indenture governing the notes does not contain any financial or operating covenants or restrictions on the payments of dividends, the incurrence of indebtedness or the issuance or repurchase of securities by us or any of our subsidiaries. The indenture contains no covenants or other provisions to afford protection to holders of the notes in the event of a fundamental change or other corporate transaction involving us except to the extent described under Description of Notes Fundamental Change Permits Holders to Require Us to Repurchase Notes, Description of Notes Conversion Rights Increase in Conversion Rate upon Conversion upon a Make-whole Fundamental Change and Description of Notes Consolidation, Merger and Sale of Assets. See also the risks described in this section under the headings We may not have the ability to raise the funds necessary to settle conversions of the notes or to repurchase the notes upon a fundamental change, and our future debt may contain limitations on our ability to make interest payments on or pay cash upon conversion or repurchase of the notes.

The increase in the conversion rate for notes converted in connection with a make-whole fundamental change may not adequately compensate you for any lost value of your notes as a result of such transaction.

If a make-whole fundamental change occurs prior to the maturity date, under certain circumstances, we will increase the conversion rate by a number of additional shares of our common stock for notes converted in connection with such make-whole fundamental change. The increase in the conversion rate will be determined based on the date on which the specified corporate transaction becomes effective and the price paid (or deemed to be paid) per share of our common stock in such transaction, as described below under Description of Notes Conversion Rights Increase in Conversion Rate upon Conversion upon a Make-whole Fundamental Change. The increase in the conversion rate for notes converted in connection with a make-whole fundamental change may not adequately compensate you for any lost value of your notes as a result of such transaction. In addition, if the price of our common stock in the transaction is greater than \$ per share or less than \$ per share (in each case, subject to adjustment), no additional shares will be added to the conversion rate. Moreover, in no event will the conversion rate per \$1,000 principal amount of notes as a result of this adjustment exceed shares of common stock, subject to adjustment in the same manner as the conversion rate as set forth under Description of Notes Conversion Rights Conversion Rate Adjustments.

Our obligation to increase the conversion rate for notes converted in connection with a make-whole fundamental change could be considered a penalty, in which case the enforceability thereof would be subject to general principles of reasonableness and equitable remedies.

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Future sales of shares of our common stock, including by us or our directors, executive officers and beneficial owners of 5% or more of our securities and their respective affiliates following expiration or early release of the lock-up or shares issued upon the exercise of currently outstanding options could cause the market price of our common stock and, in turn, the trading price of the notes, to drop significantly, even if our business is doing well.

A substantial portion of our outstanding common stock can be traded without restriction at any time. Some of these shares are currently restricted from resale as a result of securities laws, but will be able to be sold, subject to any applicable volume limitations under federal securities laws with respect to affiliate sales, in the near future. As such, sales of a substantial number of shares of our common stock in the public market could occur at any time. Sales by us or others, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. In addition, we have a significant number of shares that are subject to outstanding options. The exercise of these options and the subsequent sale of the underlying common stock could cause a further decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. In connection with this offering, we and our directors, executive officers and beneficial owners of 5% or more of our securities (other than FMR LLC, Carmignac Gestion, Capital World Investors and Ameriprise Financial, Inc.) and their respective affiliates have entered into lock-up agreements for a period of 45-days following this offering, subject to certain exceptions. We and our directors, executive officers and beneficial owners of 5% or more of our securities (other than FMR LLC, Carmignac Gestion, Capital World Investors and Ameriprise Financial, Inc.) and their respective affiliates may be released from lock-up prior to the expiration of the lock-up period at the sole discretion of RBC Capital Markets, LLC. Upon expiration or earlier release of the lock-up agreements described under the Underwriting section of this prospectus supplement, we and our directors, executive officers and beneficial owners of 5% or more of our securities (other than FMR LLC, Carmignac Gestion, Capital World Investors and Ameriprise Financial, Inc.) and their respective affiliates may sell securities into the market, which could adversely affect the market price of shares of our common stock and, in turn, the trading price of the notes. In addition, during the lock-up period and thereafter, our directors and executive officers are permitted to engage in certain market transactions for our common stock. We cannot predict the size of future issuances or the effect, if any, that this offering or any future issuances may have on the market price for our common stock or the trading price for the notes. See the risks described in this section under the heading Volatility in the market price and trading volume of our common stock could adversely impact the trading price of the notes.

The conversion rate of the notes may not be adjusted for all dilutive events.

The conversion rate of the notes is subject to adjustment for certain events, including, but not limited to, the issuance of certain stock dividends on our common stock, the issuance of certain rights or warrants, subdivisions, combinations, distributions of capital stock, indebtedness, or assets, cash dividends and certain issuer tender or exchange offers as described under Description of Notes Conversion Rights Conversion Rate Adjustments. However, the conversion rate will not be adjusted for other events, such as a third-party tender or exchange offer or an issuance of common stock for cash, that may adversely affect the trading price of the notes or our common stock. An event that adversely affects the value of the notes may occur, and that event may not result in an adjustment to the conversion rate.

Some significant restructuring transactions and significant changes in the composition of our board may not constitute a fundamental change, in which case we would not be obligated to offer to repurchase the notes.

Upon the occurrence of a fundamental change, you have the right to require us to repurchase your notes. However, the fundamental change provisions will not afford protection to holders of notes in the event of other transactions that could adversely affect the notes. For example, transactions such as leveraged recapitalizations, refinancings, restructurings, or acquisitions initiated by us may not constitute a fundamental change requiring us to repurchase the notes. In the event of any such transaction, the holders would not have the right to require us to repurchase the notes, even though each of these transactions could increase the amount of our indebtedness, or otherwise adversely affect our capital structure or any credit ratings, thereby adversely affecting the holders of notes.

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In addition, absent the occurrence of a fundamental change or make-whole fundamental change as described under Description of Notes Fundamental Change Permits Holders to Require Us to Repurchase Notes or Description of Notes Conversion Rights Adjustment to Shares Delivered upon Conversion upon a Make-whole Fundamental Change or Notice of Redemption, changes in the composition of our board of directors will not provide holders with the right to require us to repurchase the notes or to an increase in the conversion rate upon conversion.

Provisions in the indenture governing the 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 notes, holders of the notes will have the right, at their option, to require us to repurchase all or a portion of their notes. In addition, if a make-whole fundamental change occurs prior to the maturity date of the notes, we will in some cases be required to increase the conversion rate for a holder that elects to convert its notes in connection with such make-whole fundamental change. Furthermore, the indenture governing the notes prohibits us from engaging in certain mergers or acquisitions unless, among other things, the surviving entity assumes our obligations under the 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.

We cannot assure you that an active trading market will develop for the notes.

Prior to this offering, there has been no trading market for the notes, and we do not intend to apply to list the notes on any securities exchange or to arrange for quotation on any automated dealer quotation system. We have been informed by the underwriters that they currently intend to make a market in the notes after the offering is completed. However, the underwriters may discontinue their market-making at any time without notice. In addition, the liquidity of the trading market in the notes, and the market price quoted for the notes, may be adversely affected by changes in the overall market for this type of security and by changes in our financial performance or prospects or in the prospects for companies in our industry generally. As a result, we cannot assure you that an active trading market will develop for the notes. If an active trading market does not develop or is not maintained, the market price and liquidity of the notes may be adversely affected. In that case you may not be able to sell your notes at a particular time or you may not be able to sell your notes at a favorable price.

Any adverse rating of the notes may cause their trading price to fall.

We do not intend to seek a rating on the notes. However, if a rating service were to rate the notes and if such rating service were to lower its rating on the notes below the rating initially assigned to the notes or otherwise announces its intention to put the notes on credit watch, the trading price of the notes could decline.

You may be subject to tax if we make or fail to make certain adjustments to the conversion rate of the notes even though you do not receive a corresponding cash distribution.

The conversion rate of the notes is subject to adjustment in certain circumstances, including the payment of cash dividends. If the conversion rate is adjusted as a result of a distribution that is taxable to our common stockholders, such as a cash dividend, you may be deemed to have received a dividend subject to U.S. federal income tax without the receipt of any cash. In addition, a failure to adjust (or to adjust adequately) the conversion rate after an event that increases your proportionate interest in us could be treated as a deemed taxable dividend to you. If a make-whole

fundamental change occurs prior to the maturity date of the notes, under some circumstances, we will increase the conversion rate for notes converted in connection with the make-whole fundamental change. Such increase may also be treated as a distribution subject to U.S. federal income tax as a dividend. See Material U.S. Tax Considerations. If you are a non-U.S. holder (as defined in Material U.S. Tax Considerations), any deemed dividend would generally be subject to U.S. federal withholding tax at a 30% rate, or such lower rate as may be specified by an applicable treaty, which may be withheld from subsequent payments of cash and common stock payable on the notes. See Material U.S. Tax Considerations.

The capped call transactions may affect the value of the notes and our common stock.

In connection with the pricing of the notes, we expect to enter into capped call transactions with the option counterparties. The capped call transactions are expected to reduce the potential dilution and/or offset

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any cash payments due in excess of the principal amount of converted notes, as the case may be, upon any conversion of the notes, with such reduction and/or offset subject to a cap. If the underwriters exercise their over-allotment option, we may enter into additional capped call transactions.

In connection with establishing their initial hedge of the capped call transactions, the option counterparties and/or their respective affiliates expect to enter into various derivative transactions with respect to our common stock and/or purchase shares of our common stock concurrently with or shortly after the pricing of the notes. This activity could increase (or reduce the size of any decrease in) the market price of our common stock or the notes at that time.

In addition, the option counterparties and/or their respective affiliates may modify their hedge positions by entering into or unwinding various derivatives with respect to our common stock and/or purchasing or selling our common stock or other securities of ours in secondary market transactions following the pricing of the notes and prior to the maturity of the notes (and are likely to do so during any observation period related to a conversion of notes). This activity could also cause or avoid an increase or a decrease in the market price of our common stock or the notes, which could affect your ability to convert the notes and, to the extent the activity occurs during any observation period related to a conversion of notes, it could affect the number of shares and value of the consideration that you will receive upon conversion of the notes.

In addition, if any such capped call transactions fail to become effective, whether or not this offering of notes is completed, the option counterparties and/or their respective affiliates may unwind their hedge positions with respect to our common stock, which could adversely affect the value of our common stock and, if the notes have been issued, the value of the notes.

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 March 31, 2016, approximately 35.4% 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, Carmignac Gestion, Capital World Investors, Ameriprise Financial, Inc. 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 are currently subject to securities class action litigation and may be subject to similar or other litigation in the future, which may divert management's attention.

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 us and certain of our officers as defendants. These lawsuits were filed by stockholders who claim to be suing on behalf of anyone who purchased or otherwise acquired our securities between January 9, 2014 and January 10, 2014.

The lawsuits alleged that we made material misrepresentations and/or omissions of material fact in our 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 our 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

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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, we 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 into 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 million, of which \$10 million was agreed to be funded by our insurers. The settlement was paid into escrow in June 2016, with distribution to the class to occur after the Court has finally approved the settlement and a plan of allocation of those proceeds.

Under the proposed settlement, the defendants do not admit any liability. The defendants also continue to deny all allegations against them and to maintain that the suit has no merit. It is anticipated that the settlement will not have a material impact on our business.

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 have insurance, coverage could be denied or prove to be insufficient. We are not currently able to estimate the possible cost to us from these lawsuits, and we cannot be certain how long it may take to resolve these lawsuits or the possible amount of any damages that we may be required to pay. We have not established any reserves for any potential liability relating to these lawsuits. 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 on either of these lawsuits could result in the payment of substantial damages and could have a material adverse effect on our business, results of operations and financial condition. In addition, the uncertainty of the currently pending lawsuits could lead to more volatility in our stock price.

Our stock price has been and may in the future be volatile, which could cause holders of our common stock and the 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:

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

failure to successfully commercialize Ocaliva in PBC or our inability to receive marketing approval for Ocaliva in jurisdictions outside of the United States;

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 product candidates and any adverse development or perceived adverse development with respect to the regulatory review of such submission;

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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 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 or stockholder 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 are currently subject to class action securities lawsuits and may be the target of this type of litigation in the future, 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.

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We have a significant stockholder, which will limit your ability to influence corporate matters and may give rise to conflicts of interest.

Genextra S.p.A., together with its affiliates, whom we refer to collectively as Genextra, is our largest stockholder. As of March 31, 2016, Genextra owned 6,454,953 shares of our common stock. The shares of common stock owned by Genextra represented approximately 26.2% of our outstanding common stock as of March 31, 2016. Accordingly, Genextra exerts and will continue to exert significant influence over us and any action requiring the approval of the holders of our common stock, including the election of directors and amendments to our organizational documents, such as increases in our authorized shares of common stock and approval of significant corporate transactions. This concentration of voting power makes it less likely that any other holder of common stock 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 affiliated with Genextra, has the power to set the number of directors on our board from time to time.

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.

In the future, we may offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock in order to raise additional capital. 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. Investors purchasing shares or other securities in the future could have rights, preferences or privileges senior to those of existing stockholders and you may experience dilution. You may 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.

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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 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.

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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.

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

As of March 31, 2016 and December 31, 2015, we had net operating loss carryforwards, or NOLs, for federal income tax purposes of \$470.4 million and \$454.4 million, respectively, which expire between 2024 and 2036. Our ability to utilize our NOLs may be limited under Section 382 of the Internal Revenue Code of 1986, as amended, or the Internal Revenue Code. The limitations apply if an ownership change, as defined by Section 382 of the Internal Revenue Code, 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 as defined under Section 382 of the Internal Revenue Code 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 federal, state, and foreign tax purposes.

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USE OF PROCEEDS

We estimate that our net proceeds from the sale of the notes in this offering will be approximately \$ million, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their over-allotment option in full, we estimate that our net proceeds in this offering will be approximately \$ million, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use approximately \$ million of the net proceeds of this offering to pay the cost of the capped call transactions that we expect to enter into, as described under Description of Capped Call Transactions. If the underwriters exercise their over-allotment option, we may use a portion of the net proceeds from the sale of additional notes to fund our entry into additional capped call transactions.

We intend to use the remaining net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments, to fund:

the ongoing commercialization of Ocaliva in PBC in the United States;
our preparation for and, subject to receipt of marketing approval, potential initiation of the commercial launch of Ocaliva in PBC in certain European countries as well as other target markets across the world such as Canada and Australia;

the continued clinical development of OCA in PBC, NASH and PSC;
the advancement of our clinical program for INT-767; and
continued advancement of other preclinical pipeline and research and development programs.

The balance, if any, will be used for general corporate purposes, including general and administrative expenses, capital expenditures, working capital and prosecution and maintenance of our intellectual property.

We have not determined the exact amounts we plan to spend on any of the items listed above or the timing of these expenditures. Our expected use of the net proceeds from this offering represents our current intentions based upon our present plans and business conditions. We currently project adjusted operating expenses in the range of \$360 million to \$400 million in the fiscal year ending December 31, 2016, which excludes the anticipated \$45 million net expense for the settlement of the purported securities class action lawsuit, stock-based compensation and other non-cash items.

Adjusted operating expense is a financial measure not calculated in accordance with GAAP. See 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 under Risk Factors in this prospectus supplement, and our rapid growth and expansion, we currently cannot accurately or precisely predict the duration beyond 2017 over which we expect our cash and cash equivalents, including the net proceeds from this offering, to be sufficient to fund our operating expenses and capital expenditure requirements. The amounts and timing of our actual use of net proceeds will vary depending on numerous factors, including, among others, rate of progress and cost of our continued commercialization activities for Ocaliva in PBC in the United States; our ability to receive marketing approval of Ocaliva for PBC in Europe based on our regulatory submissions package and our work completed to date, such as the willingness of the EMA 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 outside of the United States if we receive marketing authorization; the progress, costs, results of and timing of our clinical development programs for OCA in PBC, NASH and other indications; the outcome, costs and timing of seeking and obtaining FDA, EMA and any other regulatory approvals; our research and development activities for our other product candidates; and other cash needs that may arise as we continue to operate our business.

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Our management will have broad discretion in the application of the net proceeds, and investors will be relying on our judgment regarding the application of the net proceeds of this offering. In addition, we might decide to postpone, modify or not pursue our commercialization plans and our research and development efforts if the net proceeds from this offering and the other sources of cash are less than expected. We have no current understandings, agreements or commitments for any material acquisitions or licenses of any products, businesses or technologies.

Pending our use of the net proceeds from this offering, we expect to invest the proceeds in short-term, interest-bearing, investment-grade securities.

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We did not record earnings for the three months ended March 31, 2016 or for the years ended December 31, 2015, 2014, 2013, 2012 or 2011. Accordingly, our earnings were inadequate to cover fixed charges for each such 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.

	Three Months Ended March 31, 2016 (in thousands) (unaudited)	Years Ended December 31,				
		2015	2014	2013	2012	2011
Deficiency	\$ (126,674)	\$ (226,429)	\$ (283,226)	\$ (67,792)	\$ (43,643)	\$ (12,738)

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.

This information should be read in conjunction with our consolidated financial statements and the accompanying notes incorporated by reference in this prospectus supplement.

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Our common stock is listed on The NASDAQ Global Select Market and trades under the symbol ICPT. The following table sets forth, for the quarterly periods indicated, the high and low sale price per share of our common stock as reported on The NASDAQ Global Select Market:

	High	Low
Year ended December 31, 2014		
First Quarter	\$ 497.00	\$ 65.22
Second Quarter	\$ 339.67	\$ 209.00
Third Quarter	\$ 349.08	\$ 208.00
Fourth Quarter	\$ 264.92	\$ 128.50
Year ended December 31, 2015		
First Quarter	\$ 308.28	\$ 144.79
Second Quarter	\$ 314.88	\$ 232.19
Third Quarter	\$ 285.00	\$ 150.00
Fourth Quarter	\$ 217.99	\$ 137.28
Year ended December 31, 2016		
First Quarter	\$ 152.60	\$ 89.76
Second Quarter (through June 28, 2016)	\$ 173.31	\$ 127.45

On June 28, 2016, the last reported sale price of our common stock on The NASDAQ Global Select Market was \$149.37 per share.

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DIVIDEND POLICY

We have never declared or paid 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.

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The following table shows our cash, cash equivalents and investment securities as well as capitalization as of March 31, 2016:

on an actual basis; and

on an as adjusted basis giving effect to the sale of \$400 million of notes offered in this offering (assuming the underwriters' over-allotment option is not exercised) and the receipt of \$ million of net proceeds, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this table together with the Use of Proceeds section in this prospectus supplement, as well as the information contained in our consolidated financial statements and condensed consolidated financial statements and related notes incorporated by reference in this prospectus supplement and the accompanying prospectus.

	March 31, 2016	
	Actual	As Adjusted ⁽¹⁾
	(unaudited, in thousands, except par value data)	
Cash, cash equivalents and investment securities	\$556,860	\$
Debt:		
% convertible senior notes due 2023 ⁽²⁾	\$	\$400,000
Total debt	\$	\$400,000
Stockholders' equity:		
Common stock, par value \$0.001 per share; 35,000,000 shares authorized and 24,594,025 shares issued and outstanding, respectively, actual and as adjusted	25	25
Additional paid-in capital ⁽²⁾	1,311,739	1,311,739
Accumulated other comprehensive income (loss), net	(1,126)	(1,126)
Accumulated deficit	(822,305)	(822,305)
Total stockholders' equity ⁽²⁾	488,333	488,333
Total capitalization	\$488,333	\$888,333

The as adjusted information does not include our entry into the capped call transactions, including our payment of approximately \$ million to fund payment of the cost of the capped call transactions, as described under (1) Description of Capped Call Transactions, which is expected to result in a reduction to our cash and cash equivalents, additional paid-in capital, stockholders' equity and total capitalization.

In accordance with ASC 470-20, a convertible debt instrument (such as the notes) that may be wholly or partially settled in cash is required to be separated into a liability and an equity component, such that interest expense reflects the issuer's nonexchangeable debt interest rate. Upon issuance, a debt discount is recognized as a decrease in debt and an increase in equity. The debt component accretes up to the principal amount over the expected term (2) of the debt. ASC 470-20 does not affect the actual amount that we are required to repay, and the amount shown in the table above for the notes is the aggregate principal amount of the notes without reflecting the debt discount or fees and expenses that we are required to recognize or the increase in paid-in capital on our consolidated balance sheet.

The table above excludes:

1,662,838 shares of common stock issuable upon the exercise of outstanding stock options as of March 31, 2016 at a weighted average exercise price of \$108.88 per share;
restricted stock units for 46,364 shares of our common stock that were unvested as of March 31, 2016;

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1,650,721 additional shares of common stock reserved for future issuance as of March 31, 2016 under our 2012 Equity Incentive Plan; and

the shares of our common stock to be reserved for issuance upon conversion of the notes being offered by us.
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DESCRIPTION OF NOTES

We will issue the notes under a base indenture to be dated as of the date of initial issuance of the notes, between us and U.S. Bank National Association, as trustee (the trustee), as supplemented by a supplemental indenture with respect to the notes. In this section, we refer to the base indenture (the base indenture), as supplemented by the supplemental indenture (the supplemental indenture), collectively as the indenture. This description of the notes supplements and, to the extent it is inconsistent, replaces the description of the general provisions of the notes and the base indenture in the accompanying prospectus. The terms of the notes include those expressly set forth in the indenture and those made part of the indenture by reference to the Trust Indenture Act of 1939, as amended (the Trust Indenture Act).

You may request a copy of the indenture from us as described under [Where You Can Find More Information](#).

The following description is a summary of the material provisions of the notes and the indenture and does not purport to be complete. This summary is subject to and is qualified by reference to all the provisions of the notes and the indenture, including the definitions of certain terms used in the indenture. We urge you to read these documents because they, and not this description, define your rights as a holder of the notes.

For purposes of this description, references to we, our and us refer only to Intercept Pharmaceuticals, Inc. and not to its subsidiaries.

General

The notes will:

- be our general unsecured, senior obligations;
 - initially be limited to an aggregate principal amount of \$400,000,000 (or \$460,000,000 if the underwriters over-allotment option is exercised in full);
 - bear cash interest from July 1, 2016 at an annual rate of % payable semiannually in arrears on January 1 and July 1 of each year, beginning on January 1, 2017;
 - be subject to redemption at our option, in whole or in part, 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 notes to be redeemed, *plus* accrued and unpaid interest to, but excluding, the redemption date;
 - be subject to repurchase by us at the option of the holders following a fundamental change (as defined below under [Fundamental Change Permits Holders to Require Us to Repurchase Notes](#)), at a fundamental change repurchase price equal to 100% of the principal amount of the notes to be repurchased, *plus* accrued and unpaid interest to, but excluding, the fundamental change repurchase date;
 - mature on July 1, 2023, unless earlier converted, redeemed or repurchased;
 - be issued in minimum denominations of \$1,000 and integral multiples of \$1,000 in excess thereof; and
 - be represented by one or more registered notes in global form, but in certain limited circumstances may be represented by notes in definitive form. See [Book-entry, Settlement and Clearance](#).
- Subject to satisfaction of certain conditions and during the periods described below, the notes may be converted at an initial conversion rate of shares of common stock per \$1,000 principal amount of notes (equivalent to an initial

conversion price of approximately \$ per share of common stock). The conversion rate is subject to adjustment if certain events occur.

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We will settle conversions of notes by paying or delivering, 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, as described under **Conversion Rights Settlement upon Conversion**. You will not receive any separate cash payment for interest, if any, accrued and unpaid to the conversion date except under the limited circumstances described below.

The indenture does not limit the amount of debt that may be issued by us or our subsidiaries under the indenture or otherwise. The indenture does not contain any financial covenants and does not restrict us from paying dividends or issuing or repurchasing our other securities. Other than restrictions described under **Fundamental Change Permits Holders to Require Us to Repurchase Notes** and **Consolidation, Merger and Sale of Assets** below and except for the provisions set forth under **Conversion Rights Increase in Conversion Rate upon Conversion upon a Make-whole Fundamental Change**, the indenture does not contain any covenants or other provisions designed to afford holders of the notes protection in the event of a highly leveraged transaction involving us or in the event of a decline in our credit rating as the result of a takeover, recapitalization, highly leveraged transaction or similar restructuring involving us that could adversely affect such holders.

We may, without the consent of the holders, reopen the indenture governing the notes and issue additional notes under the indenture with the same terms and with the same CUSIP number as the notes offered hereby (other than differences in the issue price and interest accrued prior to the issue date of such additional notes) in an unlimited aggregate principal amount; *provided* that if any such additional notes are not fungible with the notes initially offered hereby for U.S. federal securities law and federal income tax purposes, such additional notes will have a separate CUSIP number.

We do not intend to list the notes on any securities exchange or any automated dealer quotation system.

Purchase and Cancellation

We will cause all notes surrendered for payment, repurchase (including as described below), redemption, registration of transfer or exchange or conversion, if surrendered to any person other than the trustee (including any of our agents, subsidiaries or affiliates), to be delivered to the trustee for cancellation. All notes delivered to the trustee shall be cancelled promptly by the trustee. Except for notes surrendered for registration of transfer or exchange, no notes shall be authenticated in exchange for any notes cancelled as provided in the indenture.

We may, to the extent permitted by law, and directly or indirectly (regardless of whether such notes are surrendered to us), repurchase notes in the open market or otherwise, with or without notice to holders, whether by us or our subsidiaries or through a private or public tender or exchange offer or through counterparties to private agreements, including by cash-settled swaps or other derivatives. We will cause any notes so repurchased (other than notes repurchased pursuant to cash-settled swaps or other derivatives) to be surrendered to the trustee for cancellation, and they will no longer be considered outstanding under the indenture upon their repurchase.

Payments on the Notes; Paying Agent and Registrar; Transfer and Exchange

We will pay or cause the paying agent to pay the principal of, and interest on, notes in global form registered in the name of or held by The Depository Trust Company (DTC) or its nominee by wire transfer in immediately available funds to DTC or its nominee, as the case may be, as the registered holder of such global note.

We will pay the principal of any certificated notes at the office or agency designated by us for that purpose. We have initially designated the trustee as our paying agent and registrar and its corporate trust office located in the contiguous United States of America as a place where notes may be presented for payment or for registration of transfer. We may, however, change the paying agent or registrar without prior notice to the holders of the notes, and we may act as paying agent or registrar. Interest on certificated notes will be payable (i) to holders having an aggregate principal amount of \$2,000,000 or less, by check mailed to the holders of these notes and (ii) to holders having an aggregate principal amount of more than \$2,000,000, either by check mailed to each holder or, upon application by such a holder to the registrar not later than the relevant regular

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record date, by wire transfer in immediately available funds to that holder's account within the United States, which application shall remain in effect until the holder notifies, in writing, the registrar to the contrary.

A holder of notes may transfer or exchange notes at the office of the registrar in accordance with the indenture. The registrar and the trustee may require a holder, among other things, to furnish appropriate endorsements and transfer documents. No service charge will be imposed by us, the trustee or the registrar for any registration of transfer or exchange of notes, but we may require a holder to pay a sum sufficient to cover any transfer tax or other similar governmental charge required by law or permitted by the indenture. We are not required to transfer or exchange any note selected for redemption or surrendered for conversion or required repurchase.

The registered holder of a note will be treated as its owner for all purposes.

Interest and Payment Dates

The notes will bear cash interest at a rate of % per year until maturity. Interest on the notes will accrue from July , 2016, or from the most recent date on which interest has been paid or duly provided for. Interest will be payable semiannually in arrears on January 1 and July 1 of each year, beginning on January 1, 2017.

Interest will be paid to the person in whose name a note is registered at the close of business on December 15 or June 15, as the case may be, immediately preceding the relevant interest payment date (each, a regular record date). Interest on the notes will be computed on the basis of a 360-day year composed of twelve 30-day months and, for partial months, on the basis of the number of days actually elapsed in a 30-day month.

If any interest payment date, the maturity date or any earlier required repurchase date upon a fundamental change of a note falls on a day that is not a business day, the required payment will be made on the next succeeding business day and no interest on such payment will accrue in respect of the delay. The term business day means, with respect to any note, any day other than a Saturday, a Sunday or a day on which the Federal Reserve Bank of New York is authorized or required by law, regulation or executive order to close or be closed.

Unless the context otherwise requires, all references to interest in this prospectus supplement include additional interest, if any, payable at our election as the sole remedy relating to the failure to comply with our reporting obligations as described under Events of Default.

Ranking

The notes will be our general unsecured obligations that rank senior in right of payment to all of our future indebtedness that is expressly subordinated in right of payment to the notes. The notes will rank equal in right of payment with all of our existing and future liabilities that are not so subordinated. The notes will effectively rank junior to any of our secured indebtedness to the extent of the value of the assets securing such indebtedness. In the event of our bankruptcy, liquidation, reorganization or other winding up, our assets that secure secured debt will be available to pay obligations on the notes only after all indebtedness under such secured debt has been repaid in full from such assets. The notes will be structurally subordinated to all indebtedness and other liabilities incurred by our subsidiaries (including trade payables). We advise you that there may not be sufficient assets remaining to pay amounts due on any or all the notes then outstanding.

As of March 31, 2016, we had no outstanding consolidated indebtedness and total consolidated liabilities of \$105.0 million, \$4.8 million of which were owed by our subsidiaries (including trade payables), to which the notes would

have been structurally subordinated. After giving effect to the issuance of the notes (assuming no exercise of the underwriters' over-allotment option) and the use of proceeds therefrom, our total consolidated indebtedness and other liabilities would have been \$505.0 million as of March 31, 2016. Our subsidiaries have no obligation to pay any amounts due on the notes or to provide us with funds for our payment obligations under the indenture. The ability of our subsidiaries to pay dividends and make other payments to us may also be restricted by, among other things, applicable corporate and other laws and regulations, as well as agreements to which our subsidiaries may become a party. We may not be able to pay the cash portion of any conversion obligation upon conversion of the notes, to repay the notes at maturity or

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to pay cash for the fundamental change purchase price upon a fundamental change if a holder requires us to repurchase notes as described below. See Risk Factors Risks Related to the Offering and the Notes We may not have the ability to raise the funds necessary to settle conversions of the notes, to repay the notes at maturity or to repurchase the notes upon a fundamental change, and our future debt may contain limitations on our ability to pay cash upon conversion or repurchase of the notes.

Optional Redemption

No sinking fund is provided for the notes, which means that we are not required to redeem or retire the notes periodically. Prior to July 6, 2021, the notes will not be redeemable. On or after July 6, 2021, we may redeem for cash all or part of the notes, at our option, 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. In the case of any optional redemption, we will provide not less than 45 nor more than 60 calendar days notice before the redemption date by mail or electronic delivery to the trustee, the paying agent and each holder of notes, and the redemption price will be equal to 100% of the principal amount of the notes to be redeemed, *plus* accrued and unpaid interest to, but excluding, the redemption date (unless the redemption date falls after a regular record date but on or prior to the immediately succeeding interest payment date, in which case we will pay the full amount of accrued and unpaid interest to the holder of record as of the close of business on such regular record date, and the redemption price will be equal to 100% of the principal amount of the notes to be redeemed). The redemption date must be a business day.

If we decide to redeem fewer than all of the outstanding notes, the trustee will select the notes to be redeemed (in principal amounts of \$1,000 or multiples thereof) by lot, on a pro rata basis or by another method the trustee considers to be fair and appropriate.

If the trustee selects a portion of your note for partial redemption and you convert a portion of the same note, the converted portion will be deemed to be from the portion selected for redemption.

In the event of any redemption in part, we will not be required to register the transfer of or exchange any note so selected for redemption, in whole or in part, except the unredeemed portion of any note being redeemed in part.

No notes may be redeemed if the principal amount of the notes has been accelerated, and such acceleration has not been rescinded, on or prior to the redemption date (except in the case of an acceleration resulting from a default by us in the payment of the redemption price with respect to such notes).

Conversion Rights

General

Prior to the close of business on the business day immediately preceding January 1, 2023, the notes will be convertible only upon satisfaction of one or more of the conditions described under the headings Conversion upon Satisfaction of Sale Price Condition, Conversion upon Notice of Redemption, Conversion upon Satisfaction of Trading Price Condition and Conversion upon 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 all or any portion of their notes at the conversion rate at any time irrespective of the foregoing conditions. Neither the trustee nor the

conversion agent (if other than the trustee) shall have any duty to determine or verify our determination of whether any of the conditions to conversion have been satisfied.

The conversion rate for the notes will initially be shares of common stock per \$1,000 principal amount of notes (equivalent to an initial conversion price of approximately \$ per share of common stock). Upon conversion of a note, we will satisfy our conversion obligations by paying or delivering, 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, in each case, as set forth below under Settlement upon Conversion. If we satisfy our conversion obligation solely in cash or through payment and delivery, as the case may be, of a combination of cash and shares of our common stock, the amount of cash and shares of

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common stock, if any, due upon conversion will be based on a daily conversion value (as defined below) calculated on a proportionate basis for each trading day in a 20 trading day observation period (as defined below under Settlement upon Conversion). The trustee will initially act as the conversion agent.

A holder may convert fewer than all of such holder's notes so long as the notes converted are a multiple of \$1,000 principal amount.

If a holder of notes has submitted notes for repurchase upon a fundamental change, the holder may convert those notes only if that holder first withdraws its repurchase notice with respect to those notes.