2022 Annual Report

EXECUTIVE OFFICERS

Jerome Durso
President and
Chief Executive Officer

M. Michelle Berrey, M.D., M.P.H.
President of R&D and
Chief Medical Officer

David Ford
Chief Human Resources Officer

Jared Freedberg
General Counsel

Linda Richardson
Chief Commercial Officer

Andrew Saik
Chief Financial Officer

Rocco Venezia
Chief Accounting Officer

BOARD OF DIRECTORS

Paolo Fundarò
Executive Chairman
XGen Partners

Jerome Durso
President and
Chief Executive Officer

Srinivas Akkaraju, M.D., Ph.D.
Managing General Partner
Samsara BioCapital

Luca Benatti, Ph.D.
Chief Executive Officer
and Director
EryDel S.p.A.

Daniel Bradbury
Executive Chairman
Equillium, Inc.

Keith Gottesdiener, M.D.
Chief Executive Officer
and Director
Prime Medicine, Inc.

Nancy Miller-Rich
Chief Executive Officer
Miller-Rich Associates

Mark Pruzanski, M.D.
Chairman and
Chief Executive Officer
Versanis Bio

Dagmar Rosa-Bjorkeson
Chief Operating Officer
Mesoblast Limited

Gino Santini
Former SVP, Corporate Strategy
and Business Development
Eli Lilly and Company

Glenn Sblendorio
Chief Executive Officer
and Director
IVERIC bio, Inc.

COMPANY HEADQUARTERS

305 Madison Avenue
Morristown, NJ 07960
(646) 747-1000
www.interceptpharma.com

TRANSFER AGENT

VStock Transfer, LLC
18 Lafayette Place
Woodmere, NY 11598
(855) 987-8625 (Toll Free)
(212) 828-8436
www.vstocktransfer.com

INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

KPMG LLP
New York, NY

ANNUAL MEETING

The 2023 Annual Meeting of Stockholders will be held virtually on Wednesday, May 24, 2023 at www.virtualshareholdermeeting.com/ICPT2023.

Intercept's common stock trades on the Nasdaq Global Select Market under the symbol "ICPT".

If you would like a copy of any exhibit contained in the "Exhibit Index" to the Annual Report on Form 10-K, please reference the hyperlinks in our Annual Report on Form 10-K, available on www.sec.gov, or write to Investor Relations at investors@interceptpharma.com, and we will email it to you for free.

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

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2022

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to

Commission file number: 001-35668

Intercept Pharmaceuticals, Inc.
(Exact Name of Registrant as Specified in Its Charter)

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

305 Madison Avenue,
Morristown, NJ 07960
(Address of Principal Executive Offices and Zip Code)
(646) 747-1000
(Registrant's Telephone Number, Including Area Code)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	ICPT	Nasdaq Global Select Market

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

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

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

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

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

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

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

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

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

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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

The aggregate market value of the registrant's common stock held by non-affiliates as of June 30, 2022, the last business day of the registrant's most recently completed second fiscal quarter, was $335.2 million (computed by reference to the closing price of $13.81 on such date as reported by the Nasdaq Global Select Market). Common stock held by our executive officers, directors and certain stockholders as of such date has been excluded from this calculation because such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of shares of the registrant's common stock outstanding as of January 31, 2023 was 41,670,120.

DOCUMENTS INCORPORATED BY REFERENCE

Certain information required by Part III of this Annual Report on Form 10-K is incorporated by reference to the registrant's definitive proxy statement related to its 2023 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

Intercept Pharmaceuticals, Inc.
Annual Report on Form 10-K
For the Fiscal Year Ended December 31, 2022

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

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements, including, but not limited to, statements regarding the progress, timing and results of our clinical trials, including our clinical trials for the treatment of nonalcoholic steatohepatitis ("NASH"), the safety and efficacy of our approved product, Ocaliva (obeticholic acid or "OCA") for primary biliary cholangitis ("PBC"), and our product candidates, including OCA for liver fibrosis due to NASH, the timing and acceptance of our regulatory filings and the potential approval of OCA for liver fibrosis due to NASH, the review of our New Drug Application ("NDA") for OCA for the treatment of liver fibrosis due to NASH by the U.S. Food and Drug Administration (the "FDA"), our intent to work with the FDA to address the issues raised in a complete response letter ("CRL"), the potential commercial success of OCA, as well as our strategy, future operations, future financial position, future revenue, projected costs, financial guidance, prospects, plans and objectives.

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

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

- the success of our existing business and operations, including Ocaliva for PBC;
- our ability to successfully commercialize Ocaliva for PBC and, if approved, OCA for NASH;
- our ability to maintain our regulatory approval of Ocaliva for PBC;
- our ability to timely and cost-effectively file for and obtain regulatory approval of our product candidates on an accelerated basis or at all, including OCA for liver fibrosis due to NASH;
- our ability to address the issues raised in the CRL received in June 2020 with respect to OCA for NASH;
- any advisory committee recommendation or dispute resolution determination that our product candidates, including OCA for liver fibrosis due to NASH, should not be approved or approved only under certain conditions;
- any future determination that the regulatory applications and subsequent information we submit for our product candidates, including OCA for liver fibrosis due to NASH, do not contain adequate clinical or other data or meet applicable regulatory requirements for approval;
- the progress, timing, and results of our REGENERATE clinical trial, including the safety and efficacy of OCA for liver fibrosis due to NASH, and the use of a consensus panel approach to histology reads;
- our pre-submission meeting with the FDA in July 2022 in which we reviewed with the FDA the planned content and the timing of the submission of our NDA for OCA for liver fibrosis due to NASH;
- our resubmission of an NDA to the FDA for OCA for liver fibrosis due to NASH, and the potential timing, review, acceptance, and approval of the NDA;
- conditions that may be imposed by regulatory authorities on our marketing approvals for our products and product candidates, including OCA for liver fibrosis due to NASH, such as the need for clinical outcomes data (and not just results based on achievement of a surrogate endpoint), any risk mitigation programs such as a Risk Evaluation and Mitigation Strategies ("REMS") program, and any related restrictions, limitations and/or warnings contained in the label of any of our products or product candidates;
- any potential side effects associated with Ocaliva for PBC, OCA for liver fibrosis due to NASH or our other product candidates that could delay or prevent approval, require that an approved product be taken off the market, require the inclusion of safety warnings or precautions, or otherwise limit the sale of such product or product candidate, including in connection with our update to the Ocaliva prescribing information in May 2021 contraindicating Ocaliva for

patients with PBC and decompensated cirrhosis, a prior decompensation event, or compensated cirrhosis with evidence of portal hypertension;

- the initiation, timing, cost, conduct, progress and results of our research and development activities, preclinical studies and clinical trials, including any issues, delays or failures in identifying patients, enrolling patients, treating patients, retaining patients, meeting specific endpoints, or completing and timely reporting the results of our NASH or PBC clinical trials;
- the outcomes of interactions with regulators, including the FDA, regarding our clinical trials;
- our ability to establish and maintain relationships with, and the performance of, third-party manufacturers, contract research organizations and other vendors upon whom we are substantially dependent for, among other things, the manufacture and supply of our products, including Ocaliva for PBC and, if approved, OCA for liver fibrosis due to NASH, and our clinical trial activities;
- our ability to identify, develop and successfully commercialize our products and product candidates, including our ability to successfully launch OCA for liver fibrosis due to NASH, if approved;
- our ability to obtain and maintain intellectual property protection for our products and product candidates, including our ability to cost-effectively file, prosecute, defend and enforce any patent claims or other intellectual property rights;
- the size and growth of the markets for our products and product candidates and our ability to serve those markets;
- the degree of market acceptance of Ocaliva for PBC and, if approved, OCA for liver fibrosis due to NASH or our other product candidates among physicians, patients and healthcare payors;
- the availability of adequate coverage and reimbursement from governmental and private healthcare payors for our products, including Ocaliva for PBC and, if approved, OCA for liver fibrosis due to NASH, and our ability to obtain adequate pricing for such products;
- our ability to establish and maintain effective sales, marketing and distribution capabilities, either directly or through collaborations with third parties;
- competition from existing drugs or new drugs that become available;
- our ability to attract and retain key personnel to manage our business effectively;
- our ability to prevent or defend against system failures or security or data breaches due to cyber-attacks, or cyber intrusions, including ransomware, phishing attacks and other malicious intrusions;
- our ability to comply with data protection laws;
- costs and outcomes relating to any disputes, governmental inquiries or investigations, regulatory proceedings, legal proceedings or litigation, including any securities, intellectual property, employment, product liability or other litigation;
- our collaborators' election to pursue research, development and commercialization activities;
- our ability to establish and maintain relationships with collaborators with development, regulatory and commercialization expertise;
- our need for and ability to generate or obtain additional financing;
- our estimates regarding future expenses, revenues and capital requirements and the accuracy thereof;
- our use of cash, cash equivalents and short-term investments;
- our ability to acquire, license and invest in businesses, technologies, product candidates and products;
- our ability to manage the growth of our operations, infrastructure, personnel, systems and controls;
- our ability to obtain and maintain adequate insurance coverage;
- continuing threats from COVID-19, including additional waves of infections, and their impacts including quarantines and other government actions; delays relating to our regulatory applications; disruptions relating to our ongoing clinical trials or involving our contract research organizations, study sites or other clinical partners; disruptions relating to our supply chain or involving our third-party manufacturers, distributors or other distribution partners; and facility closures or other restrictions; and the impact of the foregoing on our results of operations and financial position;
- the impact of general economic, industry, market, regulatory or political conditions;

- how we use the funds received from the sale of our ex-U.S. business to Advanz Pharma and its affiliates (collectively, "Advanz");
- disagreements or legal, operational, or other business problems arising from our ongoing relationship with Advanz, including the licensing of the ex-U.S. rights to Ocaliva for PBC and, if approved, OCA for NASH, our operational separation from our former ex-U.S. commercial operations, and our agreement to supply Advanz with OCA;
- unexpected tax, regulatory, litigation, or other liabilities;
- whether we receive any future earn-outs or royalties under the transaction documents with Advanz; and
- the other risks and uncertainties identified under the captions "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this Annual Report on Form 10-K and in our other periodic filings filed with the U.S. Securities and Exchange Commission (the "SEC").

NOTE REGARDING TRADEMARKS

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

SUMMARY RISK FACTORS

Investing in our securities involves a high degree of risk. Investors should carefully consider the risks and uncertainties discussed under the caption "Risk Factors" and elsewhere in this Annual Report on Form 10-K before deciding whether to invest in our securities. The following is a list of some of these risks:

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

- We cannot be certain whether Ocaliva will receive full approval for PBC in the United States. Furthermore, OCA may not be approved on an accelerated basis, or at all, for NASH or any other indication beyond PBC and we may not receive regulatory approval for any other product candidate. Without regulatory approval, we will not be able to market and commercialize our product candidates.
- Breakthrough therapy designation for OCA may not lead to faster development or regulatory processes or increase the likelihood that the FDA will approve OCA for the treatment of NASH patients with liver fibrosis.
- We may not be able to obtain or, if approved, maintain orphan drug exclusivity for our approved products or product candidates, which could cause our revenues to suffer.

Risks Related to the Commercialization of Our Products

- Sales of Ocaliva may be adversely affected by safety and labeling changes required by regulators.
- We are subject to uncertainty relating to pricing and reimbursement. Failure to obtain or maintain adequate coverage, pricing and reimbursement for Ocaliva for PBC, OCA for liver fibrosis due to NASH, if approved, or our other future approved products, if any, could have a material adverse impact on our ability to commercialize such products.
- Legislative and regulatory healthcare reform may adversely affect our business.
- Ocaliva and our other future approved products, if any, may not achieve broad market acceptance among physicians, patients and healthcare payors, and revenues generated from their sales may be limited as a result.
- If we fail to develop OCA for additional indications such as liver fibrosis due to NASH, our commercial opportunity will be limited.

Risks Related to Clinical Trials

- We are developing product candidates for the treatment of rare diseases or diseases for which there are no or limited therapies, such as PBC and NASH, and for some of which there is little clinical experience, and our development approach involves new endpoints and methodologies. As a result, there is a heightened risk that we will not be able to gain agreement with regulatory authorities regarding an acceptable development plan, that the outcome of our clinical trials will not be favorable or that, even if favorable, regulatory authorities may not find the results of our clinical trials to be sufficient for marketing approval.
- Delays or difficulties in the commencement, enrollment and completion of our clinical trials and studies could increase our product development costs and delay, limit or prevent us from obtaining regulatory approval for OCA and our other product candidates.
- Failure can occur at any stage of clinical development. The results of earlier clinical trials are not necessarily predictive of future results and any product candidate we or our collaborators advance through clinical trials, including OCA, may not have favorable results in later clinical trials or receive or maintain regulatory approval.
- Our product candidates may have undesirable side effects which may delay or prevent marketing approval, or, if approval is received, require that our products be taken off the market or include new or additional safety warnings. Any such events may limit our existing and future product sales and materially and adversely affect our business, financial condition and results of operations.

Risks Related to Our Financial Position and Need for Additional Capital

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

- Our continuing operations have never been profitable. We expect our continuing operations 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, if at all. If adequate funds are not available to us, we may be required to delay, limit, reduce or cease our operations.
- Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Risks Related to the Transaction with Advanz

- We or Advanz may fail to perform under any of the agreements entered into in connection with the Advanz transaction, we may be subject to incremental costs related to our ongoing relationship with Advanz, and we may fail to receive certain financial benefits from the transaction. As a result, our business may be adversely affected.

Risks Related to Our Business and Strategy

- We depend on third-party contractors for a substantial portion of our operations and may not be able to control their work as effectively as if we performed these functions ourselves.
- We face rapid technological change and competition from other biotechnology and pharmaceutical companies. Our operating results will suffer if we fail to compete effectively.
- Our business and operations would suffer in the event of system failures or security or data breaches due to cyber-attacks, or cyber intrusions, including ransomware, phishing attacks and other malicious intrusions.
- We are subject to various data protection laws and our business and operations would suffer in the event of violations of these laws.

Risks Related to Our Intellectual Property

- Ocaliva's market exclusivity period will depend on the validity and enforceability of issued and pending patents covering Ocaliva.
- It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection. If our patent position does not adequately protect our products such as Ocaliva and product candidates such as OCA for liver fibrosis due to NASH, others may compete against us more directly, which could harm our business, possibly materially.
- If we do not obtain protection under the Hatch-Waxman Act in the United States (or similar legislation outside of the United States) extending the terms of our patents and/or providing data or other exclusivity for our products and product candidates, our business may be materially harmed.
- We may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights, and such litigation may divert the attention of our management and scientific personnel and adversely affect our development and commercialization efforts.

Risks Related to Our Indebtedness

- Servicing our debt will require significant amounts of cash, and we may not have sufficient cash flow from our business to effectively service our debt.
- We may incur substantially more debt or take other actions that would affect our ability to pay the principal of and interest on our debt.

Risks Related to Ownership of Our Common Stock

- We have previously been subject to securities class action litigation and may be subject to similar or other litigation in the future. Such matters can be expensive, time-consuming and have a material adverse effect on our business, results of operations and financial condition.
- Our stock price has been and may in the future be volatile, which could cause holders of our common stock to incur substantial losses.

PART I

Item 1. Business

Overview

We are a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat progressive non-viral liver diseases with high unmet medical need utilizing our proprietary bile acid chemistry. Our first marketed product, Ocaliva® (obeticholic acid or "OCA"), is a farnesoid X receptor ("FXR") agonist approved in the United States, the United Kingdom, the European Union and several other jurisdictions for the treatment of primary biliary cholangitis ("PBC") in combination with ursodeoxycholic acid ("UDCA") in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA. On July 1, 2022, we completed the sale of our ex-U.S. commercial operations to Advanz Pharma and its affiliates (collectively, "Advanz"), and sublicensed the right to commercialize Ocaliva and OCA for nonalcoholic steatohepatitis ("NASH") outside of the United States.

In addition to commercializing OCA for PBC under the Ocaliva brand name, we are also currently developing OCA for additional indications, including NASH. We are also developing product candidates in various stages of clinical and preclinical development. We believe that OCA and our other product candidates have the potential to treat orphan and other more prevalent liver diseases such as NASH for which there are currently limited therapeutic options.

Ocaliva was approved for PBC by the U.S. Food and Drug Administration ("FDA") in May 2016 under the accelerated approval pathway. We commenced sales and marketing of Ocaliva in the United States shortly after receiving approval, and Ocaliva is now available to U.S. patients primarily through a network of specialty pharmacy distributors. Ocaliva received conditional approval for PBC from the European Commission in December 2016. Since January 2017, Ocaliva has also received regulatory approval in several markets outside the United States and Europe, including (but not limited to) Canada, Israel and Australia. Ocaliva received orphan drug designation in both the United States and the European Union for the treatment of PBC. In addition, we continue to work to execute on our post-marketing regulatory commitments with respect to Ocaliva.

In June 2022, we announced topline results from our COBALT trial. The primary endpoint, as agreed with the FDA, was time to first occurrence of any of the following clinical endpoints: all-cause death, liver transplant, hospitalization for other serious liver-related events, signs of progression to hepatic decompensation, or signs of development of portal hypertension. The study did not demonstrate a statistically significant difference between Ocaliva and placebo on the primary endpoint: 71 subjects in the Ocaliva arm progressed to clinical events compared to 80 in the placebo arm ($p=0.30$; HR 0.84). The safety and tolerability of Ocaliva were consistent with its known profile and adverse events were in line with expectations for patients with advanced PBC based on the natural history of the disease. In June 2022, we also announced topline results for our HEROES-US study, a retrospective real-world study that evaluated data from a U.S. claims database, to compare clinical outcomes in a pre-defined group of patients with PBC who were treated with Ocaliva and a comparable group of PBC patients who were eligible, but who were not treated with Ocaliva. The results from the HEROES-US study showed a statistically significant and clinically meaningful reduction in all-cause death, liver transplant, or hospitalization for hepatic decompensation among Ocaliva-treated patients compared to the control group. In the Ocaliva arm ($n=429$), 8 events were observed compared to 226 in the control group ($n=4,585$) with a weighted hazard ratio of 0.38 ($p= 0.027$). HEROES-US is one of two HEROES studies we are conducting that utilizes real-world data to assess the impact of Ocaliva on clinical outcomes in PBC patients.

In September 2022, we had a supplemental NDA ("sNDA") pre-submission meeting with the FDA in which we reviewed our post-marketing requirements with respect to Ocaliva. We intend to submit the data from the COBALT and HEROES-US studies as well as additional data, including data from other real world evidence studies, as part of a broader evidence package in the sNDA in support of full approval of Ocaliva for the treatment of PBC, which we anticipate submitting to the FDA in 2023. If this data package does not support fulfillment of our post-marketing obligations, we may not be able to maintain our previously granted marketing approval of Ocaliva for PBC.

Our lead development product candidate is OCA for the potential treatment of NASH. In February 2019, we announced topline results from the planned 18-month interim analysis of our pivotal Phase 3 clinical trial of OCA in

patients with liver fibrosis due to NASH, known as the REGENERATE trial (the "Original Analysis"). The REGENERATE trial is ongoing and is expected to continue through clinical outcomes for verification and description of the clinical benefit of OCA. In June 2020, we received a complete response letter ("CRL") from the FDA stating that our NDA for OCA for the treatment of liver fibrosis due to NASH could not be approved in its present form. We had our end of review meeting with the FDA in October 2020 to discuss the FDA's risk-benefit assessment in the CRL based on its review of the available data, as well as our proposed resubmission of our NDA for the treatment of liver fibrosis due to NASH. The meeting was constructive and the FDA provided us with helpful guidance regarding supplemental data we could provide to further characterize OCA's efficacy and safety profile that could support resubmission based on our Phase 3 REGENERATE 18-month biopsy data, together with a safety assessment from our ongoing studies.

Following our end of review meeting, we had a dialogue with FDA regarding the REGENERATE study to clarify data, a new consensus read methodology for liver biopsies, and analyses required to re-submit our NDA. In connection with the resubmission of our NDA, we conducted a new interim analysis of our ongoing pivotal Phase 3 REGENERATE trial of OCA using a biopsy consensus read methodology in the same intent-to-treat ("ITT") population as the Original Analysis (the "New Interim Analysis").

In July 2022, we announced topline results from the New Interim Analysis. In this new interim analysis of the ITT population from REGENERATE, 22.4% of subjects randomized to once-daily oral OCA 25 mg met the primary endpoint of achieving at least one stage of fibrosis improvement with no worsening of NASH at month 18 on liver biopsy compared with 9.6% of subjects on placebo ($p<0.0001$). The results were consistent with the Original Analysis, which also showed that OCA 25 mg had a statistically significant effect on fibrosis improvement ($p=0.0002$). The New Interim Analysis used a consensus panel approach to histology reads, in line with recent FDA guidance, while the Original Analysis used individual central readers. A numerically greater proportion of individuals in the OCA 25 mg treatment group compared to placebo achieved the endpoint of resolution of NASH with no worsening of liver fibrosis but, consistent with the Original Analysis, the results for the endpoint of resolution of NASH were not statistically significant. As part of the New Interim Analysis, a safety evaluation was conducted in 2477 subjects from the REGENERATE trial who took at least one dose of study drug (placebo, OCA 10 mg, or OCA 25 mg). Topline results from this ongoing safety evaluation showed that treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TESAEs), and deaths were generally balanced across the OCA and placebo treatment groups in this new safety population. The most common TEAE was pruritus (24% in placebo, 33% in OCA 10 mg and 55% in OCA 25 mg) and pruritus was the most common cause for treatment discontinuation. As part of the safety review of the New Interim Analysis, independent groups of experts reviewed certain categories of safety events to provide a blinded adjudication as specifically requested by the FDA. These included events pertaining to hepatic (excluding clinical outcomes), cardiovascular and renal safety. Topline analysis through four years of treatment showed a numerically higher number of adjudicated hepatic safety events for OCA 25 mg, the majority of which were mild in severity. For adjudicated core major adverse cardiovascular events and adjudicated acute kidney injury events, frequency of events was low and balanced across treatment groups. Consistent with its mechanism of action as an FXR agonist, OCA treatment was associated with an increase in LDL at Month 1 which returned to near baseline values by Month 12. Based on the results of the New Interim Analysis, in December 2022 we re-submitted our NDA for OCA in pre-cirrhotic liver fibrosis due to NASH, which, like our original NDA submission, is for the treatment of patients with pre-cirrhotic liver fibrosis.

In July 2022, we had a pre-submission meeting with the FDA in which we reviewed the planned structure and the timing of the submission of our NDA and had an ongoing dialogue as we prepared to re-submit. The Company will need to overcome the risk-benefit assessment of the FDA from the prior review of the NDA for OCA for the treatment of liver fibrosis due to NASH. Although we believe that the insights we have gained from the re-analysis and from the larger and more robust safety database provide an improved risk-benefit, there can be no assurances that the FDA will change its view on risk-benefit and will approve such NDA on an accelerated basis, or at all.

In September 2022, we announced that REVERSE, a Phase 3 study evaluating the safety and efficacy of OCA in patients with compensated cirrhosis due to NASH, did not meet its primary endpoint of a $\geq$ 1-stage histological improvement in fibrosis with no worsening of NASH following up to 18 months of therapy. No new safety signals for OCA were observed in this population of patients with cirrhosis. In the REVERSE study of 919 randomized subjects with compensated cirrhosis due to NASH, 11.1% (p=NS) of subjects who were randomized to receive once-daily oral OCA 10 mg and 11.9% (p=NS) of subjects who were randomized to receive OCA 10 mg titrated to 25 mg (OCA 10-to-25 mg)

after three months achieved a ≥1-stage improvement in fibrosis with no worsening of NASH after up to 18 months of treatment, compared with 9.9% of subjects who received placebo. Though the REVERSE study did not succeed on the histological evaluation of the primary endpoint, a positive impact on liver stiffness as defined by transient elastography was noted in both OCA 10 mg and OCA 10-to-25 mg arms. Safety was evaluated in 916 subjects who took at least one dose of study drug (placebo, OCA 10 mg or OCA 10-to-25 mg). Treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TESAEs) and deaths were balanced across all treatment groups in REVERSE. The most common TEAE was pruritus (31% in placebo, 41% in OCA 10 mg and 57% in OCA 10-to-25 mg) and pruritus was the most common reason for treatment discontinuation. Serious gallbladder-related events were balanced across arms (0.6% in placebo, 1.0% in OCA 10 mg, 1.0% in OCA 10-to-25 mg). Consistent with the known mechanism of action of FXR-agonists, the OCA 10-to-25 mg arm had a higher incidence of gallstones.

In December 2022, we re-submitted an NDA to the FDA for OCA for the treatment of patients with pre-cirrhotic liver fibrosis due to NASH. The resubmission is supported by a robust body of evidence from the OCA NASH clinical development program, including two positive interim 18-month analyses from the pivotal Phase 3 REGENERATE study in patients with pre-cirrhotic liver fibrosis due to NASH. In both REGENERATE analyses, treatment with OCA 25 mg demonstrated a statistically significant improvement in liver fibrosis by at least one stage without worsening of NASH—an improvement that was more pronounced in individuals with more advanced disease at baseline. Other measures of liver disease, including blood levels of liver enzymes and noninvasive measures of liver stiffness, demonstrated dose-dependent improvements after 18 and 48 months of therapy. Further, a detailed analysis of the largest safety database in NASH demonstrated a monitorable and manageable safety and tolerability profile that supports the potential chronic administration of OCA.

In January 2023, we announced that the FDA accepted our NDA for OCA seeking accelerated approval for the treatment of patients with pre-cirrhotic liver fibrosis due to NASH. The FDA indicated that it considers this a complete, Class 2 resubmission and has assigned a Prescription Drug User Fee Act (PDUFA) target action date of June 22, 2023, for the NDA. The timeline for the review of the NDA by the FDA remains subject to change.

We are evaluating the efficacy, safety and tolerability of OCA in combination with bezafibrate in patients with PBC in a Phase 2 study outside of the United States that has completed enrollment. In the United States, we have an ongoing Phase 1 study to better characterize the exposure response of the fixed-dose combination, which has completed enrollment, and we have an open Investigational New Drug (“IND”) application with the FDA. We are also conducting a second Phase 2 study evaluating a fixed-dose combination of OCA and bezafibrate for the treatment of patients with PBC who have not achieved an adequate biochemical response to UDCA. Our longer-term goal is developing and seeking regulatory approval for a fixed dose combination regimen in PBC and potentially in other diseases.

In addition, we have other compounds in early stages of research and development in our pipeline, including our INT-787 compound, an FXR agonist. We are currently evaluating INT-787 in a Phase 2a clinical trial. We submitted an IND for INT-787 in the first half of 2022, which is now active.

History and Development of the Company

For a full discussion of the general development of the Company’s business, see the Company’s Annual Report on Form 10-K for the year ended December 31, 2021, which is incorporated by reference.

Key developments that have occurred since January 1, 2022 include the following:

In February 2022, the Company filed a terminal disclaimer in the United States Patent and Trademark Office concerning its RE 48,286 patent (“the '286 patent”), which is listed in the FDA Orange Book for OCALIVA. As a result of the filing, the expiration date of the '286 patent changed from November 16, 2027 to February 21, 2027.

In May 2022, the Company entered into a series of agreements to sell its ex-U.S. commercial operations, and sublicense the right to commercialize Ocaliva for PBC and OCA for NASH outside of the United States, to Advanz.

In May 2022, the Company’s stockholders approved the Company’s Amended and Restated Equity Incentive Plan.

In June 2022, the Company announced results from two studies designed to evaluate clinical outcomes in patients with PBC on Ocaliva: COBALT, a Phase 3b/4 confirmatory clinical outcomes study, and HEROES-US, one of two HEROES real-world studies. Findings from these studies are intended to be part of a broader evidence package that the Company anticipates submitting to the FDA in 2023.

In July 2022, the Company closed its previously announced transaction with Advanz.

In July 2022, the Company announced topline results from a new interim analysis of its ongoing pivotal Phase 3 REGENERATE trial of OCA in patients with liver fibrosis due to NASH.

In August 2022, we entered into a settlement agreement with Dr. Reddy's (as defined below) resolving the patent litigation over Dr. Reddy's Abbreviated New Drug Application ("ANDA") seeking approval to market a generic version of Ocaliva prior to expiration of our patents.

In September 2022, we announced that REVERSE, a Phase 3 study evaluating the safety and efficacy of OCA in patients with compensated cirrhosis due to NASH, did not meet its primary endpoint of a ≥ 1-stage histological improvement in fibrosis with no worsening of NASH following up to 18 months of therapy. No new safety signals for OCA were observed in this population of patients with cirrhosis.

In August and September 2022, we entered into a series of exchange agreements and agreed with a limited number of existing noteholders of our 2026 Convertible Secured Notes to exchange approximately $388.9 million aggregate principal amount of existing notes for $258.2 million in cash and 11,329,399 shares of newly issued common stock (equivalent to $219.4 million), for total consideration of $477.6 million. Net of these exchanges, the principal balance of the 2026 Convertible Secured Notes was reduced by $388.9 million from $500.0 million to $111.1 million. The result of these activities was to lower principal debt outstanding by 54% or $388.9 million to $336.3 million and decrease annual cash interest expense by 58% or $13.6 million to $9.8 million on an annual basis. In addition, these activities reduced overall potential shareholder dilution associated with the 2026 Convertible Secured Notes.

In December 2022, we re-submitted our NDA for OCA in pre-cirrhotic liver fibrosis due to NASH.

In January 2023, we announced that the FDA accepted our NDA for OCA seeking accelerated approval for the treatment of patients with pre-cirrhotic liver fibrosis due to NASH.

In January and February 2023, we entered into settlement agreements with five additional generic manufacturers resolving our patent litigations with them over their ANDAs seeking approval to market generic versions of Ocaliva prior to expiration of our patents.

Our Strategy

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

- *Further strengthen our foundational PBC business.* We intend to further strengthen our foundational PBC business through expanding the market for Ocaliva for eligible patients by increasing Ocaliva's market penetration. In addition, we continue to work to execute our post-marketing regulatory commitments and generate new data with respect to Ocaliva.

- *Execute our clinical and regulatory goals and timelines*. We remain focused on progressing our development program in pre-cirrhotic liver fibrosis due to NASH, including continuing our Phase 3 REGENERATE study through clinical outcomes, and pursuing regulatory approval. We also plan to advance our studies evaluating bezafibrate in combination with OCA for PBC.

- *Expand our portfolio and pipeline*. We intend to identify additional opportunities to acquire, partner on, or in-license new products and to develop OCA and our other product candidates, alone or in combination, in non-viral liver diseases. In addition, we intend to continue to advance the development of our INT-787 compound, which is an FXR agonist. We are currently evaluating INT-787 in a Phase 2a clinical trial.

- *Improve our operational and financial foundation.* We intend to maintain a strong and experienced leadership team to help to continue to drive Intercept's growth and development while prudently managing our expenses and cash position.

- *Expand and protect our intellectual property.* We intend to continue to expand and aggressively prosecute our intellectual property in the area of bile acid chemistry and therapeutics with the objective of maintaining a valuable intellectual property portfolio and to vigorously defend and enforce our intellectual property rights protecting Ocaliva.

Licenses and Collaborations

Sale of our ex-U.S. commercial operations to Advanz Pharma

On July 1, 2022, we completed the sale of our ex-U.S. commercial operations to Advanz, and sublicensed the right to commercialize Ocaliva for PBC and OCA for NASH outside of the United States. The transaction included a total upfront consideration of $405 million, subject to customary working capital and other adjustments, plus a $45 million earnout, payable upon Advanz's receipt of extensions of orphan drug exclusivity in Europe. We will also receive royalties on any future net sales of OCA in NASH outside of the U.S., should Advanz obtain marketing authorization for this indication in ex-U.S. regions. The majority of employees outside of the U.S. were transferred to Advanz, while remaining international employees continue to manage our global supply chain, support our quality organization, and support global clinical trials.

We entered into a Sublicense Agreement with Advanz (the "Sublicense Agreement") under which we agreed to continue to conduct certain post-marketing work and other activities with respect to Ocaliva for PBC, including continuing to conduct certain PBC studies (the "PBC Post-Marketing Work"). Under the terms of the Sublicense Agreement, the Company will be reimbursed by Advanz for a portion of the total R&D costs related to the PBC Post-Marketing Work.

We also entered into a Supply and Manufacture Agreement with Advanz (the "SMA") under which we have an obligation to supply Advanz with OCA in bulk tablet form and continue to be responsible for the manufacturing and supply of OCA globally while Advanz is responsible for packaging, distribution and commercialization of the therapy in all markets outside of the United States.

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

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

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

The biological effects of bile acids are mediated through dedicated receptors. The best understood receptor is FXR, a nuclear receptor that regulates bile acid synthesis and clearance from the liver, thereby preventing excessive bile acid build-up in the liver, which may be toxic. As such, FXR is a target for the treatment of several liver diseases such as PBC

that involve impaired bile flow, a condition called cholestasis. In cholestasis, the liver is typically exposed to higher than normal levels of bile acids, which can cause significant damage over time. In addition, bile acid activation of FXR is believed to induce anti-fibrotic, anti-inflammatory, anti-steatotic and other mechanisms that are necessary for the normal regeneration of the liver. As a result, FXR is also a target for the treatment of more common liver diseases such as NASH and alcoholic hepatitis. Further, based on the discovery of similar FXR-mediated protective mechanisms in other organs exposed to bile acids, we believe that FXR may also be a potential target for the treatment of a number of intestinal, kidney and other diseases.

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

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

Our First Approved Product

Ocaliva

Ocaliva was approved for PBC by the FDA in May 2016 under the accelerated approval pathway. We commenced sales and marketing of Ocaliva in the United States shortly after receiving approval, and Ocaliva is now available to U.S. patients primarily through a network of specialty pharmacy distributors. Ocaliva received conditional approval for PBC from the European Commission in December 2016. Since January 2017, Ocaliva has also received regulatory approval in several markets outside the United States and Europe, including (but not limited to) Canada, Israel and Australia. Ocaliva received orphan drug designation in both the United States and the European Union for the treatment of PBC.

Overview of PBC

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

Based on our analysis of 2016 industry data, which we believe remains a useful estimate, there were approximately 290,000 people with PBC in the United States, certain European countries, Canada, Australia and New Zealand. An estimated 90% of PBC patients are women, with approximately one in 1,000 women over the age of 40 afflicted by the disease. The mean age of diagnosis is about 40 years old and the typical initial presentation occurs between the ages of 30

and 65 years old. A majority of PBC patients are asymptomatic at the time of initial diagnosis, but most develop symptoms over time. Fatigue and pruritus are the most common symptoms in PBC patients. Less common symptoms include dry eyes and mouth, as well as jaundice, which can be seen in more advanced disease. Based on the guidelines of the American Association for the Study of Liver Disease and the European Association for the Study of the Liver, the clinical diagnosis of PBC is established based on the presence of (i) a positive antimitochondrial antibody ("AMA"), a marker of this autoimmune disease seen in up to 95% of PBC patients and (ii) elevated serum levels of ALP. In the earlier stages of PBC, ALP is often the only abnormally elevated liver enzyme, rising to between two to ten times higher than normal values. Bilirubin is a marker of liver function and is also monitored in PBC to provide an indication of how well the liver is functioning. Liver biopsy can be used to confirm the diagnosis of PBC, but is not required and is becoming less-frequently performed.

A number of published clinical studies have demonstrated that lower levels of ALP, both independently or in conjunction with normal bilirubin levels, correlate with a significant reduction in adverse clinical outcomes such as liver transplant and/or death in PBC patients. These studies include the result of meta-analyses of PBC clinical outcomes data of more than 6,000 PBC patients from 17 academic centers in eight countries that have been compiled by the Global PBC Study Group, which we sponsored, as well as a dataset of over 6,000 PBC patients across the United Kingdom compiled by the UK PBC Group.

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

Phase 3 POISE Trial

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

Following the completion of the double-blind portion of the POISE trial described above, patients were given the option to enroll in a five-year open-label long-term safety and efficacy extension trial, which has been completed. Patients received Ocaliva at a once-daily 5 mg dose for three months, after which patients were titrated based on tolerability. The data from the open-label extension portion of the trial showed that 46% of patients responded after 12 months of treatment with Ocaliva and 50% to 56% of patients responded after 48 to 72 months of treatment with Ocaliva (based on the same criteria used to define the primary endpoint in the 12 month placebo controlled trial). Reductions in ALP were sustained through the double-blind and extension portions of the trial and total bilirubin levels remained stable and within the normal range for most patients for the duration of the trial (ALP $p < 0.0001$ for all post-baseline visits; total bilirubin: p-values were not consistently significant throughout the extension portion of the POISE trial). Adverse events were consistent with the safety profile of Ocaliva in patients with PBC. The most commonly reported adverse events were pruritis and fatigue, which were generally mild to moderate in severity.

In November 2021, we presented the results of an analysis of clinical outcomes in patients with PBC treated with Ocaliva in the POISE Phase 3 study and its open label extension compared to propensity score matched external controls from the UK and Global PBC cohorts, as a late-breaking podium presentation at The Liver Meeting, the Annual Meeting

of the American Association for the Study of Liver Diseases (AASLD). The study results showed statistically significant greater transplant-free survival in patients receiving obeticholic acid as compared to the control groups.

Ongoing Confirmatory Clinical Outcomes Trial and Other Post Marketing Requirements

In connection with Ocaliva's accelerated approval in the United States and conditional approval in the European Union, in December 2014, following discussions with the FDA, we initiated our Phase 4 confirmatory outcomes trial of Ocaliva for PBC, known as the COBALT trial, and other clinical trials to satisfy post-marketing regulatory requirements. The COBALT trial was designed to evaluate subjects across the spectrum of PBC disease, including early and advanced PBC. We also agreed to evaluate the safety and efficacy of Ocaliva in patients with moderate to severe hepatic impairment in a study known as the 401 trial and as monotherapy in patients with PBC. In addition, we agreed to develop and characterize a lower dose formulation of Ocaliva to allow for once daily dosing in patients with moderate or advanced hepatic impairment. Continued approval of Ocaliva for PBC is contingent upon the verification and description of clinical benefit in the COBALT trial and our satisfaction of our other post-marketing regulatory requirements. Any delay or failure by us to satisfy such requirements may jeopardize the continued approval of Ocaliva for PBC in the United States or other jurisdictions.

The goal of the COBALT trial was to confirm that reduction of ALP based upon Ocaliva treatment is associated with a longer-term benefit on liver-related clinical outcomes. COBALT was designed to assess the effect of a once-daily dose of 5 mg or 10 mg of Ocaliva in approximately 430 PBC patients with an inadequate therapeutic response to UDCA or who were unable to tolerate UDCA. Under COBALT's previous study design, eligible patients with PBC continued their UDCA treatment, except for those patients unable to tolerate UDCA, and were randomized into one of two treatment arms of approximately 215 patients each, receiving either (i) a placebo or (ii) Ocaliva starting at 5 mg and increasing over the course of the trial to 10 mg of Ocaliva based on tolerability. Dosing frequency was determined by disease stage. The primary endpoint of the trial was based on clinical outcomes as measured by time to first occurrence of any of the following adjudicated events: death (all-cause), liver transplant, Model of End Stage Liver Disease ("MELD") score greater than 15, uncontrolled ascites or hospitalization due to variceal bleeding, hepatic encephalopathy or spontaneous bacterial peritonitis. The study was designed to evaluate subjects across the spectrum of PBC disease, including early and advanced PBC. As part of the closure of COBALT, we discussed endpoint changes with the FDA.

Further, as part of our post-marketing requirements for Ocaliva, we undertook a Phase 4 clinical trial of Ocaliva in patients with PBC who have moderate to severe hepatic impairment (Child-Pugh B and C) (known as the 401 trial). This double-blind, placebo-controlled study was designed to evaluate the pharmacokinetics of Ocaliva and its conjugates, as well as safety and tolerability. Additional objectives included an evaluation of Ocaliva treatment compared to placebo on liver biochemistry, Child-Pugh scores and non-invasive markers of liver fibrosis and stiffness. The trial as designed was targeted to enroll approximately 50 patients in the United States, Europe and other jurisdictions for 48 weeks, but ultimately enrolled a lower number of patients and was closed.

Changes to our Ocaliva label with respect to patients with PBC with decompensated cirrhosis (e.g., Child-Pugh Class B or C), a prior decompensation event, or compensated cirrhosis with evidence of portal hypertension influenced modifications to our COBALT study design, and, as a result of the changes to the U.S. prescribing information, we also removed from the trial subjects in the United States who are now excluded from the scope of the label. We also agreed with the FDA and the European Medicines Agency ("EMA") to terminate our 401 trial, in light of the exclusion of patients with PBC with decompensated cirrhosis from the Ocaliva label in the U.S. In addition, a data monitoring committee ("DMC") reviewed the unblinded results of a pre-specified interim efficacy analysis of the COBALT trial and separately reviewed unblinded safety and pharmacokinetic data from both the COBALT and 401 trials. Following these reviews, the DMC stated that it was not feasible to continue the COBALT trial as designed and noted the challenges in enrolling and maintaining placebo-controlled post-marketing studies in this rare disease setting. No acute safety concerns were noted by the DMC. Given the feasibility concerns noted by the DMC as well as the potential confounding impact of subjects discontinuing treatment and/or transitioning from investigational product to commercial drug during clinical trials, we discussed with the FDA and the EMA proposed modifications to the COBALT trial, and we notified the FDA and the EMA of the DMC's recommendation. Based on discussions with both the FDA and the EMA, we closed our COBALT and 401 trials and compiled data available from these studies.

In June 2022, we announced topline results from our COBALT trial. The primary endpoint, as agreed with the FDA, was time to first occurrence of any of the following clinical endpoints: all-cause death, liver transplant, hospitalization for other serious liver-related events, signs of progression to hepatic decompensation, or signs of development of portal hypertension. The study did not demonstrate a statistically significant difference between Ocaliva and placebo on the primary endpoint: 71 subjects in the Ocaliva arm progressed to clinical events compared to 80 in the placebo arm (p=0.30; HR 0.84). The safety and tolerability of Ocaliva were consistent with its known profile and adverse events were in line with expectations for patients with advanced PBC based on the natural history of the disease. In June 2022, we also announced topline results for our HEROES-US study, a retrospective real-world study that evaluated data from a U.S. claims database, to compare clinical outcomes in a pre-defined group of patients with PBC who were treated with Ocaliva and a comparable group of PBC patients who were eligible, but who were not treated with Ocaliva. The results from the HEROES-US study showed a statistically significant and clinically meaningful reduction in all-cause death, liver transplant, or hospitalization for hepatic decompensation among Ocaliva-treated patients compared to the control group. In the Ocaliva arm (n=429), 8 events were observed compared to 226 in the control group (n=4,585) with a weighted hazard ratio of 0.38 (p= 0.027). HEROES-US is one of two HEROES studies we are conducting that utilizes real-world data to assess the impact of Ocaliva on clinical outcomes in PBC patients. In September 2022, we had a supplemental NDA ("sNDA") pre-submission meeting with the FDA in which we reviewed our post-marketing requirements with respect to Ocaliva. We intend to submit the data from the COBALT and HEROES-US studies as well as additional data, including data from other real world evidence studies, as part of a broader evidence package in the sNDA in support of full approval of Ocaliva for the treatment of PBC, which we anticipate submitting to the FDA in 2023. If this data package does not support fulfillment of our post-marketing obligations, we may not be able to maintain our previously granted marketing approvals of Ocaliva for PBC.

Other Regulatory Information

In October 2016, the Committee for Medicinal Products for Human Use (the "CHMP") of the EMA adopted a positive opinion recommending the granting of a conditional marketing authorization of Ocaliva in PBC. Based on the CHMP's positive recommendation, the European Commission granted a conditional marketing authorization of Ocaliva in PBC in December 2016. PBC is extremely rare in the pediatric population. Therefore, in accordance with applicable regulations, the PBC marketing authorization required demonstration of compliance with all measures included in an EMA-approved Pediatric Investigation Plan for OCA for the treatment of biliary atresia, a pediatric cholestatic disease.

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

Ocaliva Label Update

In the course of our post-marketing pharmacovigilance activities, deaths have been reported in PBC patients with moderate or severe hepatic impairment. In an analysis performed by us and in consultation with the FDA, we concluded that certain of these patients were prescribed once daily doses of Ocaliva, which is seven times higher than the recommended weekly dose in such patients. As a result, in September 2017, we issued a Dear Health Care Provider ("DHCP") letter, and the FDA also subsequently issued its own drug safety communication to reinforce recommended label dosing. Both communications remind healthcare providers of the importance of the recommended reduced dosing of Ocaliva in PBC patients with moderate or severe hepatic impairment, while reiterating the importance of monitoring PBC patients for progression of their disease and the occurrence of liver-related adverse reactions. In addition to the DHCP letter, we took actions to enhance education about appropriate use of Ocaliva. These initiatives included: reeducating physicians on the label, with a focus on ensuring appropriate dosing for patients with moderate or severe hepatic impairment; enhancing monitoring of patients for liver-related adverse reactions; and adjudicating reported cases of serious liver injury, including in patients with no or mild hepatic impairment.

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

The FDA notified us that, in the course of its routine safety surveillance, in May 2020 the FDA began to evaluate a newly identified safety signal, or NISS, regarding liver disorder for Ocaliva which the FDA classified as a potential risk. The FDA informed us that its review of the NISS was focused on a subset of the cirrhotic, or more advanced, PBC patients who had taken Ocaliva. As part of our routine pharmacovigilance efforts, we worked with the FDA to reconcile our internal safety database with the FDA Adverse Event Reporting System database and we completed a comprehensive assessment of all available data, including data from our completed clinical trials, blinded reviews of ongoing clinical trial data, unblinded reviews of certain ongoing clinical trial data by the DMC, post-marketing data and natural history data, which we submitted to the FDA and had a meeting in 2021 to discuss.

In May 2021, the NISS process was concluded and we aligned with the FDA on updated Ocaliva prescribing information in the United States, and Ocaliva is now contraindicated for patients with PBC and decompensated cirrhosis, a prior decompensation event, or compensated cirrhosis with evidence of portal hypertension, in addition to the existing contraindication for complete biliary obstruction.

Our Product Candidates

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

OCA for liver fibrosis due to NASH

Our lead product candidate is OCA for the potential treatment of liver fibrosis due to NASH. In February 2019, we announced topline results from the Original Analysis of our REGENERATE trial. The REGENERATE trial, which studies subjects with pre-cirrhotic liver fibrosis due to NASH, is ongoing and is expected to continue through clinical outcomes for verification and description of the clinical benefit of OCA. In the primary efficacy analysis, once-daily OCA 25 mg met the primary endpoint agreed with the FDA of fibrosis improvement by at least one stage with no worsening of NASH at the planned 18-month interim analysis. Adverse events were generally mild to moderate in severity and the most common were consistent with the known profile of OCA. OCA has received breakthrough therapy designation from the FDA for the treatment of NASH patients with liver fibrosis. In September 2019, we submitted an NDA seeking accelerated approval of OCA for liver fibrosis due to NASH in the United States and, in December 2019, we submitted a MAA seeking conditional approval of OCA for liver fibrosis due to NASH in Europe. The FDA subsequently accepted our NDA for filing and granted a priority review designation for OCA for liver fibrosis due to NASH. In January 2020, the EMA validated our MAA and thereby confirmed that our MAA was sufficiently complete to begin the formal review process. In June 2020, we received a complete response letter ("CRL") from the FDA stating that our NDA for OCA for the treatment of liver fibrosis due to NASH could not be approved in its present form. The CRL indicated that, based on the data the FDA had reviewed, the FDA has determined that the predicted benefit of OCA based on a surrogate histopathologic endpoint remains uncertain and does not sufficiently outweigh the potential risks to support accelerated approval for the treatment of patients with liver fibrosis due to NASH. At that time, the FDA recommended that we submit additional post-interim analysis efficacy and safety data from the ongoing REGENERATE trial in support of potential accelerated approval and that the long-term outcomes phase of the trial should continue. In October 2020, we had our end of review meeting with the FDA to discuss the FDA's risk-benefit assessment in the CRL based on its review of the available data, as well as our proposed resubmission of our NDA for the treatment of liver fibrosis due to NASH. The meeting was constructive and the FDA provided us with helpful guidance regarding supplemental data we could provide to further characterize OCA's efficacy and safety profile that could support resubmission based on our Phase 3 REGENERATE 18-month biopsy data, together with a safety update from our ongoing studies.

Following our end of review meeting, we had a dialogue with FDA regarding the REGENERATE study to clarify data, a new consensus read methodology for liver biopsies, and analyses required to re-submit our NDA. In connection with the resubmission of our NDA, we conducted the "New Interim Analysis". Based on the results of the New Interim Analysis, in December 2022 we re-submitted our NDA for OCA in pre-cirrhotic liver fibrosis due to NASH.

In addition, we have conducted a number of other trials and studies in connection with our NASH development program, and announced topline data from our Phase 3 trial in NASH patients with compensated cirrhosis, known as the REVERSE trial.

Overview of NASH

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

Although difficult to precisely estimate, epidemiology research estimates that the global prevalence of NASH is approximately 3 – 5% and is expected to increase markedly by 2030. Fibrosis is the most robust predictor of long-term overall mortality, liver transplantation and liver-related events in patients with NASH and advanced fibrosis is associated with a substantially higher risk of liver-related morbidity and mortality in patients with NASH. We believe that a majority of NASH patients diagnosed and under specialist care have fibrosis of stage 2 or greater. Although the prevalence of NASH is lower in children, it has also become a serious disease burden in the pediatric population. Other common co-existing conditions such as obesity and type 2 diabetes, which are present in a majority of NASH patients, raise important risks. NASH has been linked in both developed and developing countries to the adoption of a Western diet, with increased consumption of processed foods containing polyunsaturated fatty acids and fructose.

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

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

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

Phase 3 REGENERATE Trial

We are currently conducting a pivotal Phase 3 clinical trial of OCA in patients with liver fibrosis due to NASH, known as the REGENERATE trial. REGENERATE is a randomized, double-blind, placebo-controlled, multicenter study assessing the safety and efficacy of OCA on liver-related clinical outcomes in patients with liver fibrosis due to NASH. Patients with biopsy proven NASH with fibrosis are randomized 1:1:1 to receive placebo, OCA 10 mg or OCA 25 mg once daily. In August 2019, we announced the completion of the enrollment of the clinical outcomes cohort of REGENERATE, with 2,480 adult NASH patients with fibrosis randomized at over 300 qualified centers worldwide. REGENERATE will continue through clinical outcomes for verification and description of clinical benefit. The end-of-study analysis will evaluate the effect of OCA on all-cause mortality and liver-related clinical outcomes.

An 18-month interim analysis was conducted to assess the effect of OCA in liver histology comparing month 18 biopsy with baseline. Patients without a repeat biopsy due to study discontinuation or other reason were treated as non-responders in the primary efficacy analysis and full efficacy analysis (each as described below). A smaller exploratory cohort of patients with stage 1 liver fibrosis and at least one accompanying comorbidity (specified as diabetes, obesity or alanine transaminase ("ALT") greater than 1.5 times ULN) were also enrolled in REGENERATE, but were not included in the primary efficacy analysis. As described below, these patients were included in the full efficacy analysis and safety analysis. The end-of-study analysis will evaluate the effect of OCA on all-cause mortality and liver-related clinical outcomes.

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

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

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

Fibrosis Improvement at Month 18

Primary Efficacy Analysis (ITT population: NASH with stage 2 and 3 liver fibrosis)	**Placebo n = 311**	**OCA 10 mg n = 312**	**OCA 25 mg n= 308**
Fibrosis improvement (≥ 1 stage) with no worsening of NASH*	**11.9%**	**17.6% p = 0.0446**	**23.1% p = 0.0002****
Additional Full Efficacy Analysis (ITT population plus stage 1 liver fibrosis patients)	Placebo n=407	OCA 10 mg n = 407	OCA 25 mg n = 404
Fibrosis improvement (≥ 1 stage) with no worsening of NASH*	10.6%	15.7% p = 0.0286	21% p < 0.0001
* Defined as no worsening of hepatocellular ballooning, no worsening of lobular inflammation and no worsening of steatosis.			
** Statistically significant in accordance with the statistical analysis plan agreed with the FDA.			

NASH Resolution at Month 18

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

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

Adverse events were generally mild to moderate in severity and the most common were consistent with the known profile of OCA. The frequency of serious adverse events was similar across treatment arms (11% in placebo, 11% in OCA 10 mg and 14% in OCA 25 mg) and no serious adverse event occurred in > 1% of patients in any treatment arm. There were 3 deaths (2 in placebo: bone cancer and cardiac arrest, 1 in OCA 25 mg: glioblastoma) and none were considered related to treatment.

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

Consistent with observations from previous NASH studies, OCA treatment was associated with an increase in low density lipoprotein ("LDL") cholesterol, with a peak increase of 22.6 mg/dL at four weeks and subsequently reversing and approaching baseline at month 18 (4.0 mg/dL increase from baseline). Statin therapy was initiated in 10% of placebo patients and 24% of each OCA treatment arm. Among OCA patients who initiated statins, LDL cholesterol increases reversed and fell to below baseline levels by month 6. Triglycerides rapidly and continually decreased in the OCA treatment arms through month 18. There were few and varied serious cardiovascular events and incidence was balanced across the three treatment arms (2% in placebo, 1% in OCA 10 mg and 2% in OCA 25 mg).

In patients with type 2 diabetes, OCA treatment was associated with an early transient increase in fasting glucose and hemoglobin A1c with return to levels similar to placebo by month 6. No clinically meaningful changes were noted in non-diabetic patients.

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

In July 2022, we announced topline results from the New Interim Analysis. In this new interim analysis of the ITT population from REGENERATE, 22.4% of subjects randomized to once-daily oral OCA 25 mg met the primary endpoint of achieving at least one stage of fibrosis improvement with no worsening of NASH at month 18 on liver biopsy compared with 9.6% of subjects on placebo ($p<0.0001$). The results were consistent with the Original Analysis, which also showed that OCA 25 mg had a statistically significant effect on fibrosis improvement ($p=0.0002$). The New Interim Analysis used a consensus panel approach to histology reads, in line with recent FDA guidance, while the Original Analysis used individual central readers. A numerically greater proportion of individuals in the OCA 25 mg treatment group compared to placebo achieved the endpoint of resolution of NASH with no worsening of liver fibrosis but, consistent with the Original Analysis, the results for the endpoint of resolution of NASH were not statistically significant. As part of the New Interim Analysis, a safety evaluation was conducted in 2477 subjects from the REGENERATE trial who took at least one dose of study drug (placebo, OCA 10 mg, or OCA 25 mg). Topline results from this ongoing safety evaluation showed that treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TESAEs), and deaths were generally balanced across the OCA and placebo treatment groups in this new safety population. The most common TEAE was pruritus (24% in placebo, 33% in OCA 10 mg and 55% in OCA 25 mg) and pruritus was the most common cause for treatment discontinuation. As part of the safety review of the New Interim Analysis, independent groups of experts reviewed certain categories of safety events to provide a blinded adjudication as specifically requested by the FDA. These included events pertaining to hepatic (excluding clinical outcomes), cardiovascular and renal safety. Topline analysis through four years of treatment showed a numerically higher number of adjudicated hepatic safety events for OCA 25 mg, the majority of which were mild in severity. For adjudicated core major adverse cardiovascular events and adjudicated acute kidney injury events, frequency of events was low and balanced across treatment groups. Consistent with its mechanism of action as an FXR agonist, OCA treatment was associated with an increase in LDL at Month 1 which returned to near baseline values by Month 12.

Set forth below is a summary of the New Interim Analysis from the REGENERATE trial.

	Placebo n = 311	**OCA 10 mg n = 312**	**OCA 25 mg n= 308**
At least one stage of fibrosis improvement with no worsening of NASH*	9.6%	**14.1%** p = NS	**22.4%** p < 0.0001
Resolution of NASH‡ with no worsening of liver fibrosis	3.5%	6.1% p = NS	6.5% p = NS
* Defined as no worsening of hepatocellular ballooning, no worsening of lobular inflammation and no worsening of steatosis			
‡ Defined as the overall histopathologic interpretation of (i) no fatty liver disease or (ii) fatty liver disease (simple or isolated steatosis) without steatohepatitis AND a nonalcoholic fatty liver disease (NAFLD) activity score of 0 for ballooning and 0-1 for inflammation			

In July 2022, we had a pre-submission meeting with the FDA in which we reviewed the planned structure and the timing of the submission of our NDA and had an ongoing dialogue as we prepared to re-submit. The Company will need to overcome the risk-benefit assessment of the FDA from the prior review of the NDA for OCA for the treatment of liver fibrosis due to NASH. Although we believe that the insights we have gained from the re-analysis and from the larger and more robust safety database provide an improved risk-benefit, there can be no assurances that the FDA will change its view on risk-benefit and will approve such NDA on an accelerated basis, or at all.

Phase 3 REVERSE Trial

We conducted a Phase 3 clinical trial in NASH patients with compensated cirrhosis, known as the REVERSE trial. REVERSE is a randomized, double-blind, placebo-controlled, multicenter trial evaluating the safety and efficacy of OCA in NASH patients with compensated cirrhosis. In January 2020, we announced that we completed enrollment of the REVERSE trial with over 900 patients with a biopsy-confirmed diagnosis of cirrhosis due to NASH randomized.

The primary endpoint for REVERSE is the percentage of subjects with histological improvement in fibrosis by at least one stage with no worsening of NASH using the NASH Clinical Research Network scoring system after 18 months of treatment. Patients are randomized 1:1:1 into one of three treatment arms receiving a once-daily dose of placebo, OCA 10 mg or OCA 10 mg for the first three months with titration in accordance with the study protocol up to OCA 25 mg for the remaining study period. Patients who successfully complete the double-blind phase of REVERSE will be eligible to enroll in an open-label extension phase for up to 12 additional months.

In September 2022, we announced that REVERSE, a Phase 3 study evaluating the safety and efficacy of OCA in patients with compensated cirrhosis due to NASH, did not meet its primary endpoint of a ≥ 1-stage histological improvement in fibrosis with no worsening of NASH following up to 18 months of therapy. No new safety signals for OCA were observed in this population of patients with cirrhosis. In the REVERSE study of 919 randomized subjects with compensated cirrhosis due to NASH, 11.1% (p=NS) of subjects who were randomized to receive once-daily oral OCA 10 mg and 11.9% (p=NS) of subjects who were randomized to receive OCA 10 mg titrated to 25 mg (OCA 10-to-25 mg) after three months achieved a ≥1-stage improvement in fibrosis with no worsening of NASH after up to 18 months of treatment, compared with 9.9% of subjects who received placebo. Though the REVERSE study did not succeed on the histological evaluation of the primary endpoint, a positive impact on liver stiffness as defined by transient elastography was noted in both OCA 10 mg and OCA 10-to-25 mg arms. Safety was evaluated in 916 subjects who took at least one dose of study drug (placebo, OCA 10 mg or OCA 10-to-25 mg). Treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TESAEs) and deaths were balanced across all treatment groups in REVERSE. The most common TEAE was pruritus (31% in placebo, 41% in OCA 10 mg and 57% in OCA 10-to-25 mg) and pruritus was the most common reason for treatment discontinuation. Serious gallbladder-related events were balanced across arms (0.6% in placebo, 1.0% in OCA 10 mg, 1.0% in OCA 10-to-25 mg). Consistent with the known mechanism of action of FXR-agonists, the OCA 10-to-25 mg arm had a higher incidence of gallstones.

We will continue to work with REVERSE investigators to analyze the data from both the double-blind portion of the study as well as the open-label extension phase of REVERSE.

Phase 2 CONTROL Trial

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

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

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

Phase 2 Sumitomo Dainippon Trial

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

The primary efficacy analysis was conducted on an ITT basis, testing the dose dependent effects of once daily OCA (10 mg, 20 mg and 40 mg) versus placebo on the primary endpoint.

The Sumitomo Dainippon trial did not meet statistical significance for the primary endpoint. The ITT results showed a dose dependent increase in the percentage of OCA-treated patients compared to placebo who achieved the primary endpoint ($p = 0.053$).

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

Phase 2b FLINT Trial

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

The percentage of patients meeting the primary histological endpoint, based on liver biopsies, in the FLINT trial was 45% in the OCA treatment group and 21% in the placebo group ($p = 0.0002$, $n = 219$). The mean pre-treatment baseline NAS for patients in the OCA treatment group was 5.3 of a total possible score of eight (comprised of a NAS of 0-2 for hepatocellular ballooning, 0-3 for lobular inflammation and 0-3 for steatosis).

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

OCA treatment was associated with serum lipid changes, including increases in total cholesterol and LDL cholesterol and a decrease in HDL cholesterol, that developed within 12 weeks of treatment initiation, then reversed through the end of treatment and returned to baseline during the 24-week post-treatment follow-up phase. Based on these observations, lipid management was emphasized partway into the trial, using accepted guidelines. At 72 weeks as compared to baseline, the following effects were observed in the OCA treatment group: an increase in mean total cholesterol (0.16 mmol/L or 6 mg/dL increase OCA versus 0.19 mmol/L or 7mg/dL decrease placebo, $p = 0.0009$), an increase in mean LDL cholesterol (0.22 mmol/L or 9 mg/dL increase OCA versus 0.22 mmol/L or 8 mg/dL decrease placebo, $p < 0.0001$), a decrease in mean HDL cholesterol (0.02 mmol/L or 1 mg/dL decrease OCA versus 0.03 mmol/L or 1 mg/dL increase placebo, $p = 0.01$) and a decrease in triglycerides (0.22 mmol/L or 20 mg/dL decrease OCA versus 0.08 mmol/L or 7 mg/dL decrease

placebo, p = 0.88, not significant). These changes in cholesterol levels, along with the achievement of predefined efficacy criteria, played a role in the decision of the FLINT data and safety monitoring board to terminate the treatment phase of the FLINT trial, and the publication of the FLINT results noted the need for further study of these changes.

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

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

OCA and Bezafibrate

In December 2018, we entered into an agreement (the "Aralez Agreement") with Aralez Pharmaceuticals Canada Inc. ("Aralez"), pursuant to which we acquired (i) Aralez's license to develop and commercialize bezafibrate in the United States (as amended and restated in connection therewith, the "Bezafibrate License"), (ii) Aralez's IND on file with the FDA and other associated regulatory documentation and (iii) a non-exclusive license to certain of Aralez's intellectual property. Pursuant to the Aralez Agreement, we paid $9.0 million to Aralez in connection with the closing of the transactions in December 2018 and are obligated to make a $2.0 million milestone payment to Aralez based on the occurrence of specified regulatory-related events. Pursuant to the Bezafibrate License, we are also obligated to make a $2.5 million milestone payment based on the occurrence of specified regulatory-related events with respect to such a combination product, as well as mid-single digit percentage royalty payments based on the net sales of such a combination product.

Bezafibrate, a PPAR agonist that has been studied in PBC, is not approved in the U.S. for any indication. We are evaluating the efficacy, safety and tolerability of OCA in combination with bezafibrate in patients with PBC in a Phase 2 study outside of the United States that has completed enrollment. In the United States, we have an ongoing Phase 1 study to better characterize the exposure response of the fixed-dose combination, which has completed enrollment, and we have an open IND application with the FDA. We are also conducting a second Phase 2 study evaluating a fixed-dose combination of OCA and bezafibrate for the treatment of patients with PBC who have not achieved an adequate biochemical response to UDCA. Our longer-term goal is developing and seeking regulatory approval for a fixed dose combination regimen in PBC and potentially in other diseases.

Other Product Candidates

The discovery and development of safe and effective new product candidates and the development of additional uses for our existing product candidates and approved products, are important for the continued strength of our business. We, together with our collaborators, have discovered several bile acid chemistry-based compounds that are in the early stages of research and development. Among these compounds is INT-787, which is an FXR agonist that we are currently evaluating in a Phase 2a clinical trial. We submitted an IND for INT-787 in the first half of 2022, which is now active. INT-787 has distinct pharmacological properties that differ from those of OCA and has shown potential anti-fibrotic and anti-inflammatory effects in animal models. We believe that bile acid analogs may have utility in a broad range of diseases

beyond non-viral liver disease and we have in the past, and may in the future, explore the potential application of our development compounds outside of our core areas of focus. In a Phase 1, double-blind, placebo-controlled, single-ascending dose (SAD) and multiple-ascending dose (MAD) study, subjects were randomized to receive INT-787 or placebo (6:2 allocation) in each dose cohort. The study randomized and dosed 130 subjects. Safety and tolerability were assessed based on adverse events, laboratory assessments, electrocardiograms (ECGs), vital signs, and physical examinations. Results showed INT-787 was generally well tolerated in healthy subjects. No serious adverse events were reported. The majority of treatment-emergent adverse events were mild, and no treatment-limiting adverse events were identified. Mild pruritus was reported in 3 of 130 subjects. INT-787 showed rapid absorption with peak plasma concentration at 2 hours post-dose, and exposure increased in a dose-dependent manner. The half-life of total INT-787 ranged from 20 to 43 hours in cohorts with robust exposure. Renal excretion of conjugated INT-787 was observed in urine PK. The apparent steady state for total INT-787 concentration was reached by day 7 in the MAD study. As of February 2023, we had completed recruitment of our Phase 1 study.

In November 2022, we announced plans to focus development of INT-787 in severe alcohol-associated hepatitis (sAH). Alcohol-related liver disease is currently the leading indication for liver transplant listing in the U.S., with a marked increase in patients with sAH needing liver transplantation. Currently, there are no medicines with an approved indication to treat sAH. Initial data from the Phase 1 trial of INT-787 in healthy subjects supported a favorable safety and tolerability profile for INT-787 in healthy male and female adults. The Company has also initiated the FRESH (FXR Effect on Severe Alcohol-Associated Hepatitis) study, a Phase 2a trial evaluating the safety, tolerability, efficacy and pharmacokinetics of INT-787 in subjects with sAH. The Phase 2a FRESH study is a randomized, double-blind, dose-escalation study that is expected to enroll approximately 50 patients with sAH across multiple clinical sites in the U.S., UK and France. The study aims to demonstrate and provide rationale for the selection of optimal dose(s) of INT-787 in the target patient population. INT-787 will be evaluated for safety and tolerability prior to dose escalation. Overall early efficacy, based on the Lille score at Day 7 compared to placebo, will be assessed for each dose cohort, as well as change in MELD score and mortality.

The process from discovery to development to regulatory approval of a product candidate can take more than ten years. Product candidates can fail at any stage of the process, and product candidates may not receive regulatory approval even after many years of research and development and significant investment. In addition, we may decide to terminate or deprioritize the development of our product candidates due to a number of factors, including our views of the relevant regulatory development pathway, competitive landscape, commercial viability of the product candidate, or superior alternative uses of capital. For example, we have studied OCA for primary sclerosing cholangitis (“PSC”), a rare, serious, chronic cholestatic liver disease characterized by a progressive, autoimmune-based destruction of bile ducts with eventual onset of cirrhosis. While we believe that the results of our Phase 2 AESOP trial announced in 2017 established a proof of concept of OCA in a second cholestatic liver disease, we have deprioritized development of OCA in PSC based, in part, on the lack of clarity on the regulatory pathway for this rare but serious disease. In addition, we are no longer actively developing INT-767, an orally administered dual FXR and TGR5 agonist derived from the primary human bile acid chenodeoxycholic acid.

Competition

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

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

Ocaliva for PBC

Ocaliva is indicated for the treatment of PBC in combination with UDCA in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA. UDCA is a first-line therapy approved for the treatment of PBC that is available generically at a significantly lower cost than Ocaliva. Additional product candidates in Phase 3 or earlier clinical or preclinical development for the treatment of PBC include Genfit SA's dual PPAR alpha/delta agonist (elafibranor) (which has been licensed to Ipsen Pharma for worldwide commercialization, excluding China, Hong Kong, Taiwan, and Macau), CymaBay's PPAR delta agonist (seladelpar), Calliditas Therapeutics' NOX 1/4 inhibitor (setanaxib), Zydus' dual PPAR α/γ agonist (saroglitizar), Genkyotex's NOX1/NOX4 inhibitor (setanaxib), Mirum Pharmaceuticals' IBAT inhibitor (volixibat), and Cour Pharmaceuticals' and Ironwood Pharmaceuticals' PDC-E2 candidate (CNP104). Additionally, several companies have product candidates aimed at the cholestatic-induced pruritus associated with PBC, including apical sodium dependent bile acid transport inhibitors being developed by GlaxoSmithKline plc (GSK2330672).

Off-label uses of other potential treatments may also compete with Ocaliva for PBC. For example, while fibrates are not approved for use in PBC, off-label use of fibrate drugs has been reported. Bezafibrate, a fibrate that is not approved by the FDA for any indication and is only available outside of the United States, has been studied in PBC. Although we have a license to develop and commercialize bezafibrate in the United States, bezafibrate has been studied in multiple clinical trials for the treatment of liver diseases including PBC and NASH outside of the United States.

OCA for Liver Fibrosis Due to NASH

There are currently no medications approved for the treatment of NASH. However, various therapeutics are used off-label for the treatment of NASH, primarily to manage common comorbidities associated with NASH, including vitamin E (an antioxidant), insulin sensitizers (e.g., metformin, pioglitazone), antihyperlipidemic agents (e.g., gemfibrozil), and hemorrheologic agents (e.g., pentoxifylline). Although none of these treatments have been clearly shown in clinical trials to alter the course of the disease, in a previous study conducted by the NASH Clinical Research Network, improvements in certain histological measures of NASH were reported with vitamin E and pioglitazone. There are several product candidates in Phase 3 or earlier clinical or preclinical development for the treatment of NASH, including Madrigal Pharmaceuticals, Inc.'s ("Madrigal's") THR beta agonist (resmetirom), Novo Nordisk's GLP-1 agonist (semaglutide), Akero Therapeutics' FGF21 agonist (efruxifermin), Inventiva's pan-PPAR agonist (lanifibranor), AstraZeneca's GLP-1/GCGR agonist (cotadutide), 89bio's pegozafermin, Viking Therapeutics' THR beta agonist (VK29098), and Axcella Health's EMM composition of amino acids and derivatives (AXA1125), as well as FXR agonists from Novartis AG (tropifexor, nidufexor), Metacrine (MET409, MET642), Terns Pharmaceuticals (TERN-101), and Enanta Pharmaceuticals, Inc. (EDP-305), and Gilead Sciences, Inc. and Novo Nordisk's combination FXR agonist/ACC inhibitor (cilofexor/firsocostat). NASH is a multifactorial disease and consequently we believe that several treatment options may be necessary to manage the disease effectively.

On December 19, 2022, Madrigal announced the topline results of its Phase 3 clinical trial of resmetirom for treatment of NASH, meeting its dual primary endpoints of NASH resolution with ≥ 2-point reduction in NAS and no worsening of fibrosis, and ≥ 1-stage improvement in fibrosis with no worsening of NAS, and its key secondary endpoint of LDL-C lowering. According to Madrigal, resmetirom was safe and well-tolerated at both doses tested, and the frequency of serious adverse events was similar across treatment arms. Madrigal announced that in the first half of 2023 it intends to file a new drug application seeking Subpart H accelerated approval of resmetirom. The success of Madrigal or another competitor in treating NASH could adversely affect the market for OCA, even if OCA is approved.

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

Intellectual Property

Protecting our intellectual property, such as our patents, is a key part of our strategy. We are the owner of record of numerous issued U.S. patents and non-U.S. patents (some of which are sublicensed to Advanz, for which we remain responsible for patent filing, prosecution and maintenance, pursuant to the terms of our Sublicense Agreement with Advanz) with claims directed to pharmaceutical compounds, pharmaceutical compositions, methods of making these compounds and methods of using these compounds in various indications. In addition, we are the owner of record of numerous pending U.S. and non-U.S. patent applications, and regularly pursue additional patent applications in various jurisdictions. We also have numerous trademark and service mark registrations and pending trademark and service mark applications in the United States and abroad.

The patent portfolio for OCA contains U.S. and non-U.S. patents and patent applications directed to compositions of matter, methods of use and manufacturing methods. Our primary composition of matter patent for OCA was to expire in 2022. In light of the U.S. marketing approval of Ocaliva for PBC in May 2016, we applied for an extension of the patent term for this patent in the United States into 2027, which extension has been granted. In February 2022, we filed a terminal disclaimer in the United States Patent and Trademark Office concerning our primary composition of matter patent for OCA, which changed the expiration date of the patent from November 16, 2027 to February 21, 2027.

The table set forth below summarizes the U.S. patents covering OCA that are listed in the FDA's Orange Book List of Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"). The issued patents covering OCA are expected to expire in 2027 at the earliest and 2036 at the latest if the appropriate maintenance, renewal, annuity, or other government fees are paid. We expect that the patents in the OCA portfolio that are listed in the Orange Book would expire as set forth below, assuming the appropriate maintenance, renewal, annuity or other governmental fees are paid.

Patent No.	Brief Summary of Patent	U.S. Patent Expiration
RE 48,286	Claims OCA compound	2027
9,238,673	Claims OCA active pharmaceutical ingredient ("API")	2033
10,047,117	Claims methods of treating FXR mediated diseases with OCA API	2033
10,052,337	Claims OCA finished drug product	2036
10,174,073	Claims OCA API produced by a specified process	2033
10,751,349	Claims OCA finished drug product	2036
10,758,549	Claims methods of treating PBC with OCA	2036

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

We may rely on trade secrets to protect our proprietary technologies, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to protect our trade secrets and other proprietary information. We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems.

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

very similar or identical to ours. The patent positions of pharmaceutical companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States or in foreign jurisdictions, and the legal standards relating to the patentability, validity and enforceability of pharmaceutical patents are evolving.

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

We have received paragraph IV certification notice letters from seven generic drug manufacturers indicating that each such manufacturer submitted to the FDA an ANDA seeking approval to manufacture and sell a generic version of our 5 mg and 10 mg dosage strengths of Ocaliva for PBC prior to the expiration of certain patents listed for Ocaliva in the Orange Book.

The seven generic drug manufacturers and when we received their initial paragraph IV certification notices are as follows: (1) Apotex Inc. ("Apotex") (July 2020), (2) Lupin Limited ("Lupin") (July 2020), (3) Amneal Pharmaceuticals of New York, LLC, as U.S. agent for Amneal EU Limited (collectively, "Amneal") (July 2020), (4) Optimus Pharma Pvt Ltd ("Optimus") (July 2020), (5) MSN Pharmaceuticals Inc. and MSN Laboratories Private Limited (collectively, "MSN") (July 2020), (6) Dr. Reddy's Laboratories, Inc., and Dr. Reddy's Laboratories, Ltd. (collectively, "Dr. Reddy's") (December 2020), and (7) Zenara Pharma Private Limited ("Zenara") (August 2022).

Each paragraph IV certification notice alleged that the challenged Orange Book patents were invalid, unenforceable, and/or would not be infringed by the commercial manufacture, use, or sale of the generic products described in the generic manufacturer's respective ANDA. In each case, within 45 days of receipt of the paragraph IV certification notice, we initiated a patent infringement suit against the generic manufacturer in the United States District Court for the District of Delaware.

We entered into settlement agreements with Apotex, Lupin, Amneal, Optimus, MSN and Dr. Reddy's. Those settlements fully resolved the patent infringement case in the United States District Court for the District of Delaware that was scheduled for trial on February 27, 2023, and the case was terminated by the Court. Separate patent litigation against Zenara remains pending in the District of Delaware, with trial scheduled for July 22, 2024. Under the Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Act"), the FDA cannot grant final approval of the Zenara ANDA before the earlier of February 8, 2025, or a court decision in its favor. Under the terms of the six settlement agreements, we granted each of the manufacturers a non-exclusive, non-sublicensable, non-transferable, royalty-free license to commercialize a generic version of Ocaliva in the United States commencing on a specified date, or earlier under certain circumstances. The earliest such specified date agreed to is September 1, 2031 (for Apotex).

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

Manufacturing and Supply

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

We source the manufacture and commercial supply of API from such manufacturers, for use in Ocaliva and, if approved, OCA for liver fibrosis due to NASH. We believe that we have secured supplies of API sufficient to meet our

PBC commercial supply requirements as well as our NASH commercial supply requirements during the initial stages of our NASH launch if OCA is approved for the treatment of liver fibrosis due to NASH, and we have the ability to leverage potential supply from multiple qualified suppliers of API for the manufacture of Ocaliva and, if approved, OCA for liver fibrosis due to NASH. If OCA is approved for liver fibrosis due to NASH, we may be obligated to purchase a portion of our API requirements from one such supplier.

We do not have long-term supply agreements for any of our product candidates other than OCA, and regularly obtain supplies and services relating to our product candidates from third-party contract manufacturers on a purchase order basis. Contract manufacturers are subject to extensive governmental regulation and we depend on them for compliance with the requirements of U.S. and non-U.S. regulators for the manufacture of our finished products, including Ocaliva. We intend to continue to rely on third-party manufacturers for the manufacture of clinical supplies of our product candidates and commercial supplies of our approved products, including Ocaliva and, if approved, OCA for liver fibrosis due to NASH. We believe this manufacturing strategy will enable us to direct financial resources to the development and commercialization of products rather than diverting resources to establishing a manufacturing infrastructure.

Sales and Marketing

Ocaliva is our first approved product and the commercial launch of Ocaliva for PBC was our first product launch. We are commercializing Ocaliva for PBC using a combination of our internal commercial organization and third-party distributors. We are developing our commercialization strategy for OCA for liver fibrosis due to NASH, if approved, and have not yet decided on our commercialization strategy for OCA for other indications or for our other product candidates, in each case, if approved. We intend to continue to evaluate how best to commercialize our product candidates, if approved, and may choose to collaborate with third parties that have sales and marketing capabilities and established distribution systems, either to augment our own capabilities or in lieu thereof.

Customers

We commenced our commercial launch of Ocaliva for the treatment of PBC in the United States in June 2016. In December 2016, the European Commission granted conditional approval for Ocaliva for the treatment of PBC. Since January 2017, Ocaliva has also received regulatory approval in several markets outside the United States and Europe, including (but not limited to) Canada, Israel and Australia. We recognized net product sales of Ocaliva of $285.7 million, $260.8 million and $234.0 million for the years ended December 31, 2022, 2021 and 2020, respectively. We sell Ocaliva to a limited number of specialty pharmacies which dispense the product directly to patients. The specialty pharmacies are referred to as our customers. For a discussion of our customer concentration, see Note 2 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Government Regulation and Product Approval

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

United States Government Regulation

NDA Approval Processes

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

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice regulations;
- submission to the FDA of an IND, which must take effect before human clinical testing may begin;
- approval by an independent institutional review board ("IRB"), representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices ("GCP") to establish the safety and efficacy of the new drug product for each indication for which FDA approval is sought;
- preparation and submission to the FDA of an NDA;
- review of the new drug product by an FDA advisory committee, where appropriate or if applicable, although the FDA is not bound by the recommendation of an advisory committee;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the new drug product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices ("cGMP") requirements and to assure that the facilities, methods and controls are adequate to preserve the new drug product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCP and the integrity of the clinical data;
- payment of user fees and procurement of FDA approval of the NDA; and
- compliance with any post-approval requirements, including, as applicable, Risk Evaluation and Mitigation Strategies ("REMS") and post-approval studies required by the FDA.

Preclinical and Clinical Studies

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

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCPs. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, research subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and progress reports detailing the status of the clinical trials must be submitted to the FDA

annually. Sponsors also must timely report to the FDA serious and unexpected adverse reactions, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigation brochure, or any findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug. An IRB at each institution must, among other things, review and approve the protocol before a clinical trial commences at such institution, and approve the consent form that must be provided to each research subject or the subject's legal representative, monitor the study until completed and otherwise comply with regulations applicable to the IRB.

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

- *Phase 1.* The drug is initially introduced into healthy human subjects and tested to assess pharmacological actions, safety, dosage tolerance, absorption, metabolism, distribution and elimination and, in some cases, early evidence of effectiveness. In the case of some products intended for the treatment of severe or life-threatening diseases, such as cancer, especially when the product may be inherently too toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

- *Phase 2.* Clinical trials are performed on a limited patient population intended to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- *Phase 3.* Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population generally at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product and provide an adequate basis for product labeling, should it ultimately be approved for marketing. In most cases the FDA requires two adequate and well-controlled Phase 3 clinical trials with statistically significant results to demonstrate the efficacy of the drug. A single Phase 3 clinical trial with other confirmatory evidence may be sufficient in certain instances.

Human clinical trials are inherently uncertain and Phase 1, Phase 2 and Phase 3 testing may not be successfully completed. The FDA or the sponsor may suspend a clinical trial at any time for a variety of reasons, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. In some cases, clinical trials are overseen by an independent group of qualified experts organized by the trial sponsor, or the clinical monitoring board or data monitoring committee. This group typically provides recommendations to the trial sponsor for whether or not a trial may move forward at designated check points. These decisions are based on the data monitoring committee's independent review of data from the ongoing trial.

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

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

Concurrent with clinical trials, sponsors usually complete additional animal safety studies and also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing commercial quantities of the product in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug and the manufacturer must develop methods for testing the quality, purity and potency of the drug prior to release. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its proposed shelf-life.

The results of product development, nonclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests and other control mechanisms, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of user fees, but a waiver of such fees may be obtained under specified circumstances. Currently, the application fee is approximately $3.2 million for NDAs with clinical data and approximately $1.6 million for NDAs without clinical data. The sponsor under an approved NDA is also subject to annual program user fees, currently approximately $394,000. Program fees are assessed for each approved prescription drug product identified in an approved application, up to five program fees per application. These fees are typically modified annually. The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. It may request additional information rather than accept an NDA for filing. In this event, the NDA must be re-submitted with the additional information. The re-submitted application also is subject to review before the FDA accepts it for filing.

Once the NDA is accepted for filing, the FDA begins an in-depth review. NDAs receive either standard or, as discussed more fully below, priority review. The FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data. Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. The FDA reviews an NDA to determine, among other things, whether a product is safe, effective, and can be properly manufactured for its intended use or uses. The FDA may refer the NDA to an advisory committee for review and recommendation as to whether the application should be approved and under what conditions, although the FDA is not bound by the recommendation of an advisory committee. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured and tested to ensure compliance with cGMPs. An approval letter from the FDA authorizes commercial marketing of the product and specifies the prescribing information for the approved indication(s).

Fast Track, Breakthrough Therapy, Priority Review and Accelerated Approval

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

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

A product may also be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

The FDA may also designate a product for priority review if it would provide a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention of a serious condition. Certain other applications may also qualify

for priority review. The FDA determines, on a case-by-case basis, whether the proposed drug represents a significant improvement when compared with other available therapies. A priority designation by the FDA is intended to direct the agency's attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

In addition, the FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval. In the case of unprecedented accelerated approval endpoints, this determination occurs during the review of the NDA. Unless otherwise informed by the FDA, an applicant must submit to the FDA for consideration during the preapproval review period copies of all promotional materials, including promotional labeling as well as advertisements, intended for dissemination or publication within 120 days following marketing approval. After 120 days following marketing approval, unless otherwise informed by the FDA, the applicant must submit promotional materials at least 30 days prior to the intended time of initial dissemination of the labeling or initial publication of the advertisement.

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

See "Item 1. Business—Overview" for discussion of our accelerated approval status.

Post-approval Requirements

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

Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with cGMP and other laws. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

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

These sanctions could include:

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

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

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

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

Risk Evaluation and Mitigation Strategy

The Food and Drug Administration Amendments Act of 2007 created a new section of the FDCA which authorizes the FDA to require a REMS as a condition of NDA approval, or based upon new safety information regarding an approved drug, when the FDA determines a REMS is necessary to ensure that the benefits of a drug outweigh the potential risks. Under a REMS, the FDA may require various measures to address serious risks, such as medication guides, communication plans, training or registries, as well as steps to monitor and assess the effectiveness of those measures. Such requirements may impose significant burdens on prescribers, pharmacists or patients. The requirement for a REMS may materially affect the potential market and profitability of a drug.

Patent Term Extension and Data Exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use of our drug candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, (the "Hatch-Waxman Act"). The Hatch-Waxman Act permits an extension of a patent term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, the extension of patent term cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term extension period is generally one-half the time between the effective date of an IND (or, if later, the grant date of the patent), and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for extension must be made prior to expiration of the patent. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

Data exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is considered a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance as further defined in FDA regulations. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application ("ANDA") or a 505(b)(2) NDA for a drug with the same active moiety. However, an application may be submitted four years from the NDA approval date if it contains a paragraph IV certification that a reference product patent is invalid or not infringed by the ANDA or 505(b)(2) product. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an approved NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the original active moiety for other conditions of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA may be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric Exclusivity and Pediatric Use

In the United States, under the Best Pharmaceuticals for Children Act, sponsors may obtain a six month extension of unexpired regulatory exclusivities and terms of unexpired Orange Book-listed patents relating to their drug, if pediatric studies substantially complying with a Written Request are completed and submitted by the sponsor to the FDA within the statutory time frame.

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

Orphan Drug Designation

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

If a product that has orphan drug designation subsequently receives the first FDA approval for an indication of an orphan-designated condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any applications from any other party to market the same drug for the same indication for seven years, except in very limited circumstances such as where there is a demonstration of clinical superiority. Orphan drug exclusivity, however, could also work to block the approval of one of our product candidates for seven years if a competitor develops the same drug as one of our product candidates and obtains approval and orphan exclusivity for the same indication or disease for which our product candidate is being developed. Orphan drug exclusivity would not block approval of the same drug developed by a competitor for a use different from our orphan-protected approved use. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to orphan exclusivity for the full scope of its approved use.

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

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

Regulation Outside of the United States

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

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

Prior to obtaining a marketing authorization in the European Union submitted as a full stand-alone dossier, applicants have to demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan ("PIP") covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver, or (3) a deferral for one or more of the measures included in the PIP. In the case of orphan medicinal products, completion of an approved PIP can result in an extension of the aforementioned market exclusivity period from ten to twelve years.

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

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

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

Pricing and Reimbursement

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

Third-party payers are responsible for managing overall pharmaceutical drug spending for their client membership. Third-party payers continue to scrutinize and manage the prices charged for pharmaceutical products and services, and many also limit reimbursement for newly-approved or innovating products and indications. If these third-party payors do not consider our products to be cost-effective compared to other therapies, they may (i) not cover our approved products

as part of their plans' benefits, (ii) apply utilization management restrictions or high patient cost-sharing obligations or (iii) restrict the level of reimbursement for our approved products and any such actions may affect our ability to sell our approved products on a profitable basis or at all.

Medicare is a U.S. federal healthcare program that provides coverage for certain healthcare items and services to individuals aged 65 years or older, as well as individuals of any age with certain disabilities and illnesses. The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA") imposed new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries. Under Part D of the MMA, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which provide coverage for outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as part of Medicare Advantage plans. Unlike Medicare Part A and B, Part D prescription drug plan sponsors are not required to pay for all outpatient drugs, and each Part D plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D plan drug formularies must include at least two drugs within each therapeutic category and class of Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutics committee. Part D plan coverage and reimbursement may increase demand for our products for which we receive marketing approval in the United States. Moreover, while Part D provides prescription drug benefits only to Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in reimbursement by Medicare may result in a similar reduction in payments from non-governmental payors. Medicare Part D may affect reimbursement of our products upon approval.

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

In addition to the Medicaid Drug Rebate Program, federal law requires companies to participate in the Public Health Service's 340B Drug Pricing Program in order to have the manufacturer's drugs covered under Medicaid. The 340B Drug Pricing Program requires participating manufacturers to charge statutorily-defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010 (collectively, the "ACA"), extended eligibility to participate in the 340B program to certain additional types of hospitals (including critical access hospitals, sole community hospitals, rural referral centers and freestanding cancer hospitals). For purposes of these newly eligible covered entities, the ACA specifically excluded from the definition of "covered outpatient drugs" certain drugs designated as "orphan drugs" under section 526 of the FDCA. We are also required as a condition of Medicaid participation to discount our products to authorized users of the Federal Supply Schedule of the General Services Administration, including the TRICARE retail pharmacy program, under which additional laws and requirements apply.

These programs require submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, and the guidance governing such calculations is not always clear. Compliance with such requirements can require significant investment in personnel, systems and resources, but failure to properly calculate prices, or offer required discounts or rebates can subject manufacturers to substantial penalties.

In 2010, the ACA was enacted to, among other things, expand access and increase consumer insurance protections while reducing the cost of health care for consumers. The law substantially changed the way health care is financed by both governmental and private insurers in the United States. The ACA requires manufacturers to provide discounts on the prices of brand named drugs in the coverage gap under Medicare Part D and increased the rebates paid by pharmaceutical companies on drugs covered by Medicaid. The ACA also imposes an annual fee, which increases each year, on sales by branded pharmaceutical manufacturers. The ACA has been challenged repeatedly in court, and its future is uncertain. If the ACA is ultimately overturned or repealed, the effect on our business could be material.

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

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

U.S. Fraud and Abuse Laws

Interactions and arrangements with third-party payors, healthcare providers and professionals and customers, including patients and patient advocacy groups, are subject to broadly applicable fraud and abuse and other healthcare laws and regulations that may restrict certain marketing and contracting practices. These laws include, federal and state anti-kickback and false claims statutes as well as other statutes and regulations pertaining to healthcare fraud and abuse. Other pharmaceutical companies have settled alleged or admitted violations of these fraud and abuse laws with state and federal authorities in recent years and in some cases these settlements have amounted to hundreds of millions, or even billions, of dollars in damages, fines, and penalties, as well as the imposition of compliance program obligations through Corporate Integrity Agreements and other means. Lawsuits, or enforcement actions brought under fraud and abuse laws, can be extremely costly to defend, even if a company has strong defenses and ultimately succeeds in getting the allegations or enforcement action dismissed.

The federal Anti-Kickback Statute (42 U.S.C. §1320a-7b(b)) prohibits, among other things, knowingly and willfully soliciting, receiving, offering or providing remuneration, directly or indirectly, to induce either the referral of an individual, or the furnishing, recommending, or arranging for any good or service, for which payment may be made under federal and state healthcare programs such as Medicare, Medicaid or other federally financed healthcare programs. Remuneration is not defined in the federal Anti-Kickback Statute and has been broadly interpreted by regulators to include for example, cash payments, gifts, discounts, coupons, and the furnishing of free or discounted services or supplies, and other items or services of value to the recipient. This statute has been broadly interpreted to apply to manufacturer arrangements with prescribers, purchasers, formulary managers and patients, among others. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for such exceptions or safe harbors.

The federal False Claims Act imposes civil penalties, including treble damages and significant per-claim penalties, which may be pursued through civil whistleblower or *qui tam* actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. The government and *qui tam* relators have brought False Claims Act actions against pharmaceutical companies on the theory that their practices

have caused false claims to be presented to the government. There is also a separate false claims provision imposing criminal penalties.

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

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

Other Laws

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

The federal Physician Payments Sunshine Act requirements under the ACA, and its implementing regulations, require manufacturers of drugs, devices, biologics and medical supplies to report to the U.S. Department of Health and Human Services information related to certain direct and indirect payments and other transfers of value made to covered recipients, such as physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Payments made to physicians and research institutions for clinical trials are included within the ambit of this law. We may also be subject to similar laws in various states or foreign jurisdictions. Some jurisdictions' laws are broader in scope than federal laws.

In addition, several states now require prescription drug companies to report expenses relating to the marketing and promotion of drug products. Several states prohibit providing certain payments or items of value to healthcare providers or other enumerated individuals or entities, as well as various other marketing-related activities. Certain states require the posting of information relating to clinical studies and their outcomes. In addition, several states require pharmaceutical companies to implement compliance programs and marketing codes, and additional states are considering similar proposals. Also, some states and localities require sales representatives to be registered or licensed. Some of the state laws are broader in scope than federal laws. Compliance with these laws is challenging and requires significant time and resources, and any failure to comply with such laws could result in significant civil penalties and other adverse consequences.

Human Capital Resources

As of December 31, 2022, we had 341 employees, of which 331 were based in the United States, including at our facilities in New Jersey and San Diego, and 10 were based outside the United States, including at our offices in London. A significant percentage of our employees have obtained advanced degrees in their professions. None of our employees are represented by a labor union and we consider our employee relations to be good.

We consider the intellectual capital of our employees to be an essential driver of our business and key to our future prospects. Given our leadership in the treatment of progressive non-viral liver disease coupled with our disciplined management of our financial resources, we continue to be able to fill the vacated positions and, if needed, grow our headcount in support of our commercial organization and our pipeline of research and development programs and product

candidates. In addition, we continually evaluate our headcount with respect to our business needs and opportunities and seek to balance in house expertise and capacity with outsourced expertise and capacity.

We monitor our compensation programs closely and provide what we consider to be a competitive mix of compensation and insurance benefits for our employees, as well as participation in our equity programs.

We offer employees a number of additional resources and tools to help in their personal and professional development, including career development planning, professional assessment and feedback tools, and wellness programs through which employees may access information regarding scheduled healthy lifestyle activities, articles and other beneficial resources.

We are committed to hiring, developing and supporting a diverse and inclusive workplace, and continue to focus on extending our equality, diversity and inclusion initiatives across our workforce. Our virtual Diversity, Equity, and Inclusion (DEI) Hub recognizes the power of a diverse, equitable and inclusive work force, and how it enriches the professional lives of team members, drives innovation, and connects the Company to the patients and communities it serves. Employees have access to internally produced resources, articles, and toolkits, as well as a virtual DEI calendar.

Corporate and Available Information

We were incorporated in Delaware in September 2002. Our principal executive offices are located at 305 Madison Avenue Morristown, NJ 07960 and our telephone number is (646) 747-1000. We have several additional offices, including those in San Diego, California and London, United Kingdom.

Our corporate website address is *www.interceptpharma.com*. We make available on our website, free of charge, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission ("SEC"). Our SEC reports can be accessed through the Investors & Media section of our internet website. The references to *www.interceptpharma.com* herein are inactive textual references only, and the information found on our internet website is not incorporated by reference into this Annual Report on Form 10-K or any other report we file with or furnish to the SEC. The SEC maintains an internet website that contains reports, proxy and information statements and other information about issuers, like us, that file electronically with the SEC. The address of that site is *http://www.sec.gov.*

Item 1A. Risk Factors

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

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

We cannot be certain whether Ocaliva will receive full approval for PBC in the United States. Furthermore, OCA may not be approved on an accelerated basis, or at all, for NASH or any other indication beyond PBC and we may not receive regulatory approval for any other product candidate. Without regulatory approval, we will not be able to market and commercialize our product candidates.

The development, testing, manufacture, packaging, labeling, storage, approval, promotion, advertising, distribution, marketing and export and import, among other things, of our products and product candidates are subject to extensive regulation by the FDA in the United States. We are not permitted to market our product candidates in the United States until we receive approval of an NDA from the FDA. Currently, our ability to generate product sales depends on the successful marketing of Ocaliva for PBC. In the future, our ability to generate product sales in addition to those of Ocaliva for PBC will depend on whether we are successful in obtaining regulatory approval of our other product candidates, including OCA for liver fibrosis due to NASH.

Ocaliva is our only drug that has been approved for sale and it has only been approved for the treatment of PBC in combination with UDCA in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA. In the United States, Ocaliva was approved for PBC under the accelerated approval pathway. Accelerated approval was granted for Ocaliva for PBC based on a reduction in ALP; however, continued approval of Ocaliva for PBC in the United States is contingent upon the verification and description of clinical benefit in confirmatory trials and our satisfaction of our other post-marketing regulatory requirements. Any failure by us to confirm the clinical benefit of Ocaliva for PBC due to COVID-19 or other factors may jeopardize the continued approval of Ocaliva for PBC.

In addition, we continue to work to execute on our post-marketing regulatory commitments with respect to Ocaliva. In June 2022, we announced topline results from our COBALT trial. The primary endpoint, as agreed with the FDA, was time to first occurrence of any of the following clinical endpoints: all-cause death, liver transplant, hospitalization for other serious liver-related events, signs of progression to hepatic decompensation, or signs of development of portal hypertension. The study did not demonstrate a statistically significant difference between Ocaliva and placebo on the primary endpoint: 71 subjects in the Ocaliva arm progressed to clinical events compared to 80 in the placebo arm (p=0.30; HR 0.84). The safety and tolerability of Ocaliva were consistent with its known profile and adverse events were in line with expectations for patients with advanced PBC based on the natural history of the disease. In June 2022, we also announced topline results for our HEROES-US study, a retrospective real-world study that evaluated data from a U.S. claims database, to compare clinical outcomes in a pre-defined group of patients with PBC who were treated with Ocaliva and a comparable group of PBC patients who were eligible, but who were not treated with Ocaliva. The results from the HEROES-US study showed a statistically significant and clinically meaningful reduction in all-cause death, liver transplant, or hospitalization for hepatic decompensation among Ocaliva-treated patients compared to the control group. In the Ocaliva arm (n=429), 8 events were observed compared to 226 in the control group (n=4,585) with a weighted hazard ratio of 0.38 (p= 0.027). HEROES-US is one of two HEROES studies we are conducting that utilizes real-world data to assess the impact of Ocaliva on clinical outcomes in PBC patients.

In September 2022, we had an sNDA pre-submission meeting with the FDA in which we reviewed our post-marketing requirements with respect to Ocaliva. We intend to submit the data from the COBALT and HEROES-US studies as well as additional data, including data from other real world evidence studies, as part of a broader evidence package in the

sNDA in support of full approval of Ocaliva for the treatment of PBC, which we anticipate submitting to the FDA in 2023. If this data package does not support fulfillment of our post-marketing obligations, we may not be able to maintain our previously granted marketing approval of Ocaliva for PBC.

Ocaliva is not approved for any indication other than PBC. We currently have no other products approved for sale and we cannot guarantee that we will ever have additional marketable products or that OCA will be approved for use in additional indications such as NASH. NDAs must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety and effectiveness for each desired indication. NDAs must also include significant information regarding the chemistry, manufacturing and controls for the product. Obtaining approval of an NDA is a lengthy, expensive and uncertain process, and we may not be successful in obtaining approval. The FDA review processes can take years to complete and approval is not guaranteed. Even after the submission of an NDA, the FDA may decide not to accept the submission for filing and review or may determine that the submission does not support approval. For example, in 2020 we received a CRL from the FDA with respect our NDA for OCA for liver fibrosis due to NASH. The CRL indicated that, based on the data the FDA had reviewed, the FDA determined that the predicted benefit of OCA based on a surrogate histopathologic endpoint remained uncertain and did not sufficiently outweigh the potential risks to support accelerated approval for the treatment of patients with liver fibrosis due to NASH.

In July 2022, we had a pre-submission meeting with the FDA in which we reviewed the planned structure and the timing of the submission of our NDA and had an ongoing dialogue as we prepared to re-submit. The Company will need to overcome the risk-benefit assessment of the FDA from the prior review of the NDA for OCA for the treatment of liver fibrosis due to NASH. Although we believe that the insights we have gained from the re-analysis and from the larger and more robust safety database provide an improved risk-benefit, there can be no assurances that the FDA will change its view on risk-benefit and will approve such NDA on an accelerated or conditional basis, or at all.

In order to obtain and/or maintain regulatory approval for OCA for indications other than PBC, we will need to complete additional clinical trials and studies. For example, we re-submitted our NDA for OCA for patients with pre-cirrhotic liver fibrosis following the results of the New Interim Analysis in December 2022, but we can provide no assurances that the FDA will grant approval. Our ability to obtain and maintain the regulatory approvals necessary to commercialize OCA for indications other than PBC, including NASH, will depend on our ability to successfully design, conduct and complete these trials, the efficacy, safety and risk-benefit profile of OCA demonstrated by such trials and our ability to prepare and submit complex regulatory filings in accordance with applicable regulatory requirements.

There can be no assurance that Ocaliva will receive full approval from the FDA or that OCA will receive marketing approval on an accelerated or conditional basis, or at all for NASH, or that any of our other product candidates will receive marketing approval for any indication in any jurisdiction. We cannot predict whether our clinical trials and studies for our product candidates, including OCA for NASH or any other indication, will be successful, whether regulatory authorities will agree with our conclusions relating to the clinical trials and studies we conduct, or whether such regulatory authorities will require us to conduct additional clinical trials or studies.

For example, while OCA received breakthrough therapy designation from the FDA in January 2015 for the treatment of NASH patients with liver fibrosis and we re-submitted our NDA for OCA for pre-cirrhotic liver fibrosis due to NASH following the results of the New Interim Analysis in December 2022, we do not know if the FDA will approve OCA for liver fibrosis due to NASH on an accelerated or conditional basis, or at all.

If we are unable to obtain or maintain regulatory approval for OCA for PBC or for other indications, we may not be able to generate sufficient revenue to maintain profitability or to continue our operations.

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

If a drug is intended for the treatment of a serious or life-threatening condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development, the FDA may grant a breakthrough therapy designation. Breakthrough therapy designation is intended to facilitate the development, and

expedite the review, of such drugs, but the breakthrough therapy designation does not assure marketing approval by the FDA.

In January 2015, we received breakthrough therapy designation for OCA for the treatment of NASH patients with liver fibrosis. However, there is no guarantee that the receipt of breakthrough therapy designation will result in a faster development process, review or approval of OCA for liver fibrosis due to NASH or increase the likelihood that OCA will be granted marketing approval for NASH patients with liver fibrosis. Notwithstanding our receipt of breakthrough therapy designation, in June 2020 we received a CRL from the FDA with respect to our NDA for OCA for liver fibrosis due to NASH. Although we re-submitted our NDA seeking accelerated approval of OCA for the treatment of pre-cirrhotic liver fibrosis due to NASH to the FDA in December 2022, there is no assurance that the issues identified in the CRL will be satisfactorily resolved or that our NDA will be approved. Similarly, any future breakthrough therapy designation relating to any other potential indication of OCA or our other product candidates will neither guarantee a faster development process, review or approval nor improve the likelihood of the grant of marketing approval by the FDA compared to conventional FDA procedures. In addition, the FDA may withdraw any breakthrough therapy designation at any time. While we may seek breakthrough therapy designation for one or more of our product candidates in the future, we can give no assurance that the FDA will grant such status.

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

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

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

In September 2021, the United States Court of Appeals for the Eleventh Circuit decided in *Catalyst Pharmaceuticals, Inc. v. FDA* that the FDA's interpretation of orphan drug exclusivity "for the same drug for the same disease or condition" as meaning the same "use or indication" was inappropriately narrow. This decision had the potential to significantly broaden the scope of orphan drug exclusivity for drugs that receive marketing approval for orphan indications that are narrower than their orphan-designated conditions in the United States. On January 24, 2023, the FDA issued a statement to address the uncertainty created by the circuit court's decision in *Catalyst*. This notification announced that, at this time, in matters beyond the scope of that court order (i.e., ordering the FDA to set aside its approval of the specific drug at issue), the FDA intends to continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved. We cannot guarantee which rules and interpretations will be governing going forward in different situations, that the FDA will maintain this current position, or that other judicial actions will not impact the FDA's application of the Orphan Drug Act.

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

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

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

We rely on our suppliers for the manufacture and commercial supply of API for use in Ocaliva and, if approved, OCA for liver fibrosis due to NASH. We are currently dependent upon a limited number of suppliers, with whom we have contractual arrangements, although we are working on developing further sources of supply. While we have procured supplies of API for the commercialization of Ocaliva for PBC and, if approved, OCA for liver fibrosis due to NASH that we believe will be sufficient to meet our requirements during the initial stages of a potential NASH launch, we may not be able to procure sufficient supplies of API on an ongoing basis. If these suppliers are unable to provide adequate supply, we may not be able to meet our long-term commercial supply requirements of API for the manufacture of Ocaliva or, if approved, OCA for liver fibrosis due to NASH or other indications on acceptable terms, or at all. Under the SMA with Advanz, we also have an obligation to supply Advanz with OCA in bulk tablet form. If we encounter supply chain delays or are unable to procure sufficient supplies of OCA, we may not be able to fulfill our supply obligations to Advanz under the SMA and this could also impact the fulfillment of our own supply needs for OCA. We do not have agreements for long-term supplies of any of our product candidates other than OCA. We currently obtain supplies and services relating to our other product candidates from our third-party contract manufacturers on a purchase order basis.

The facilities used by any contract manufacturer to manufacture OCA or any of our other product candidates are subject to inspection by the FDA and regulators in other jurisdictions, as are the facilities and operations of our third-party vendors and CROs. We are completely dependent on these third-party manufacturers for compliance with the requirements of U.S. and non-U.S. regulators for the manufacture of our finished products, including Ocaliva. If our manufacturers are unable to meet our requirements in accordance with our product specifications and applicable current Good Manufacturing Practices ("cGMP") requirements, our products or product candidates will not be approved or, if already approved, may be subject to recall. In addition, if COVID-19 or related public health safety measures prevent the FDA or other relevant regulators from conducting manufacturing inspections or other regulatory activities with respect to manufacturing, it could significantly impact the ability of the FDA or such other regulators to timely review and process our regulatory submissions, which could have a material and adverse effect on our business and financial condition.

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

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

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

We depend on third-party vendors and CROs for certain of our clinical trial and product development activities. If any of these providers fail to comply with their contractual commitments or applicable regulatory obligations, including the completion of deliverables in a timely manner and in accordance with acceptable quality standards, including due to supply chain or business disruptions due to pandemics, geopolitics, or otherwise, our business could be materially and adversely affected. In addition, if we are unable to maintain our relationship with any one or more of these providers, we could experience a significant delay in both identifying another comparable provider and then contracting for its services, which could materially and adversely affect our clinical trial and product development efforts. We may be unable to retain an alternative provider on reasonable terms, or at all. Even if we locate an alternative provider, it is likely that such a provider will need additional time to respond to our needs and may not provide the same type or level of services as the original provider. Any third-party vendors and CROs that we retain are subject to the FDA's regulatory requirements and similar foreign standards and we do not have control over compliance with these regulations by these providers. The FDA and other relevant regulatory authorities enforce these regulations through periodic inspections of trial sponsors, principal investigators and trial sites. If these regulations are not adhered to by these providers, or if such providers fail to timely correct any non-compliance, or if COVID-19 or related public health safety measures prevent the FDA or other relevant regulatory authorities from conducting inspections or other regulatory activities, the commercialization and development of our product candidates or approved products could be delayed, which could materially and adversely harm our business and financial condition.

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

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

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

- issue Form 483 notices or Warning Letters, in the case of the FDA, or similar notices, in the case of other regulatory agencies;

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

- require us or our collaborators to enter into a consent decree or permanent injunction, which may include the imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;

- recall or hold our products;

- suspend any of our ongoing clinical studies;

- impose administrative, civil or criminal penalties;

- withdraw regulatory approval or require changes to our product label, including the inclusion of additional warnings or changes to the approved indication;

- refuse to approve pending applications or supplements to approved applications filed by us or our collaborators;

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

- seize or detain products.

Risks Related to the Commercialization of Our Products

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

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

In 2020 the FDA notified us that, in the course of its routine safety surveillance, in May of that year it began to evaluate a newly identified safety signal, or NISS, regarding liver disorder for Ocaliva which the FDA classified as a potential risk, focused on a subset of the cirrhotic, or more advanced, PBC patients who had taken Ocaliva. In May 2021, the NISS process was concluded and we aligned with the FDA on updated Ocaliva prescribing information in the United States, and Ocaliva is now contraindicated for patients with PBC and decompensated cirrhosis, a prior decompensation event, or compensated cirrhosis with evidence of portal hypertension, in addition to the existing contraindication for complete biliary obstruction. This issue, and any other safety concerns associated with Ocaliva, perceived or real, may adversely affect the successful development and commercialization of our product candidates and approved products, including Ocaliva, and materially and adversely affect our business including future revenue generated by Ocaliva.

Regulators other than the FDA may also require safety and labeling changes.

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

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

For example, our former affiliate in France (which we sold to Advanz on July 1, 2022), had initiated sales of Ocaliva prior to finalization of reimbursement terms, and, in February 2022, withdrew its reimbursement application for Ocaliva for treatment of PBC, on account of inability to reach mutually acceptable pricing terms with French regulators, which we expect to result in a partial payback of past reimbursements. Responsibility for the payback was transferred to Advanz, and reflected in a purchase price adjustment based on the expected payback, although we remain responsible for reimbursing Advanz if the final amount agreed with French regulators (attributable to the period prior to the sale of the affiliate to Advanz) is greater than the expected payback.

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

The Inflation Reduction Act, referred to as the IRA, was recently signed into law by President Biden, which makes significant changes to how drugs are covered and paid for under the Medicare program, including the creation of financial penalties for drugs whose prices rise faster than the rate of inflation, redesign of the Medicare Part D program to require manufacturers to bear more of the liability for certain drug benefits, and government price-setting for certain Medicare Part D drugs, starting in 2026, and Medicare Part B drugs starting in 2028. We have evaluated, and will continue to evaluate, the effect of the IRA on our business. At this time, we do not expect the IRA to have a material effect.

We do not know if Ocaliva for PBC will obtain and maintain broad acceptance from third-party payors in the jurisdictions in which it is, or may in the future be, approved. In addition, even if OCA for liver fibrosis due to NASH is approved, we do not know if it will obtain and maintain broad acceptance from third-party payors. The coverage determination process is a time-consuming and costly process that requires us to provide scientific and clinical support for the use of Ocaliva for PBC and, if approved, OCA for liver fibrosis due to NASH to each payor separately, with no

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

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

Legislative and regulatory healthcare reform may adversely affect our business.

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

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act (collectively, the "ACA"), became law in the United States. Among other things, the purpose of the ACA was to reduce the cost of healthcare and substantially change the way healthcare is financed by both governmental and private insurers. The ACA requires discounts under the Medicare drug benefit program and increased the rebates paid by pharmaceutical companies on drugs covered by Medicaid. The ACA also imposes an annual fee, which increases each year, on sales by branded pharmaceutical manufacturers. The ACA has been challenged repeatedly in court, and its future is uncertain. If the ACA is ultimately overturned or repealed, the effect on our business could be material.

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

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

by the pharmaceutical industry may be further exacerbated by legislative and policy changes proposed or considered by the executive branch and the United States Congress. We cannot predict the success or impact of any such current or future federal or state legislative efforts.

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

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

In addition, we continue to closely evaluate the impact of COVID-19 on our ability to effectively market, sell and distribute Ocaliva for PBC. The long-term effects of COVID-19 are unknown.

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

- limitations, warnings, precautions, boxed warnings, contraindications, restrictions or other statements contained in the product labels of our products, or any risk mitigation programs such as a REMS required for our products by the FDA, EMA or other relevant regulatory authorities;
- changes in the standard of care or availability of alternative therapies at similar or lower costs for the targeted indications for any of our products, such as UDCA for the treatment of PBC;
- limitations in the approved indications for our products;
- demonstrated and perceived clinical safety and efficacy compared to competitive products;
- a lack of adverse side effects, including deaths and other serious adverse events;
- sales, marketing and distribution support;
- the availability of reimbursement from managed care plans and other third-party payors;
- the timing of the market introduction of competitive products;
- the degree of cost-effectiveness;
- availability of alternative therapies at similar or lower cost, including generic and over-the-counter products;
- the extent to which our products are approved for inclusion on formularies of hospitals and managed care organizations;
- whether and to what extent our products are recommended under physician treatment guidelines for the treatment of the indications for which we have received regulatory approval;
- adverse publicity concerning our products or favorable publicity concerning competitive products;

- the convenience and ease of administration of our products;
- potential product liability claims; and
- the effects of COVID-19 and related public health safety measures and business closures and disruptions.

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

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

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

Physicians are permitted to prescribe drug products for uses that are not described in the product's labeling and that differ from those approved by the FDA or other applicable regulatory agencies. Off-label uses are common across medical specialties. Although the FDA and other regulatory agencies do not regulate a physician's choice of treatments, the FDA and other regulatory agencies do restrict communications on the subject of off-label use. Companies are not permitted to promote drugs in a manner inconsistent with applicable regulatory guidance. The FDA, the U.S. Department of Justice ("DOJ") and other regulatory and enforcement authorities actively enforce laws and regulations prohibiting the improper promotion of approved products, as well as the promotion of products for which marketing approval has not been obtained. A company that is found to have improperly promoted off-label uses will be subject to significant liability, including civil and administrative remedies as well as criminal sanctions. A significant number of pharmaceutical companies have received inquiries or been the subject of investigations by various governmental authorities in the United States and abroad. Both federal and state governments have levied large civil and criminal fines against companies for alleged improper off-label promotion, as well as promotion that is determined to be false or misleading, even if related to approved indications.

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

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

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

Federal false claims laws generally prohibit anyone from knowingly and willingly presenting, or causing to be presented, any claims for the payment for goods (including drugs) or services to third-party payers (including Medicare and Medicaid) that are false or fraudulent. The federal civil monetary penalties statute, likewise, imposes penalties against any person or entity that, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to generate business, including the purchase or prescription of a particular product covered by Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers or formulary managers on the other. Although there are several statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exemption or safe harbor. In addition, such exemptions and safe harbors are subject to change from time to time.

The Health Insurance Portability and Accountability Act of 1996 (as amended by the Health Information Technology for Economic and Clinical Health Act, "HIPAA") created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or obtain, by means of false or fraudulent pretenses, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. HIPAA also imposes significant requirements on the receipt and transfer of protected health information.

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

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

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

A number of pharmaceutical and other healthcare companies have been prosecuted under these laws for a variety of promotional and marketing activities, including providing free trips, free goods, sham consulting fees and grants and other monetary benefits to prescribers; reporting inflated average wholesale prices that were then used by federal programs to

set reimbursement rates; engaging in improper promotional activities; and submitting inflated best price information to the Medicaid Drug Rebate Program to reduce liability for Medicaid rebates.

If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including criminal and significant civil penalties, damages, fines, imprisonment, exclusion of products from reimbursement under United States federal or state healthcare programs, and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could materially and adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with these laws may prove costly.

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

Developing pharmaceutical products, conducting clinical trials, obtaining regulatory approval, expanding manufacturing capabilities and marketing approved products are expensive, complex and time-consuming undertakings. As a result, we have in the past entered into, and may in the future seek to enter into, collaborations with third parties upon whom we may rely for financial resources and for development, regulatory and commercialization expertise for selected products or product candidates and in selected jurisdictions. We may establish collaborations with respect to the development and commercialization of OCA in various jurisdictions and for our other product candidates. Additionally, we may enter into sales and marketing arrangements with third parties with respect to our approved products in all or certain jurisdictions.

Our collaborators may fail to develop our product candidates or effectively commercialize our products for a variety of reasons, including a lack of sufficient resources, a decision not to devote the necessary resources due to internal constraints, such as limited cash or human resources, a change in strategic focus or a failure to obtain the necessary regulatory approvals.

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

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

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

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

The completion of development, securing of approval and commercialization of OCA for additional indications such as liver fibrosis due to NASH will require substantial additional funding, is subject to numerous risks and we may not be successful. We cannot provide you any assurance that we will be able to successfully advance any of these indications through the development process. Even if we receive regulatory approval to market OCA for the treatment of liver fibrosis due to NASH or any other additional indications, we cannot assure you that any such additional indications will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives. If we are unable to successfully develop and commercialize OCA for liver fibrosis due to NASH or other additional indications, our commercial opportunity will be limited and our business prospects will suffer.

Risks Related to Clinical Trials

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

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

In the United States, the FDA generally requires two adequate and well-controlled pivotal clinical trials to approve an NDA. Furthermore, for full approval of an NDA, the FDA requires a demonstration of efficacy based on a clinical benefit endpoint. The FDA may grant accelerated approval based on a surrogate endpoint reasonably likely to predict clinical benefit. Even though our pivotal clinical trial for a specific indication, such as our Phase 3 REGENERATE trial of OCA in patients with liver fibrosis due to NASH, may achieve its primary endpoints and is reasonably believed by us to be likely to predict clinical benefit, the FDA may not accept the results of such trial or approve our product candidate on an accelerated basis, or at all. It is also possible that the FDA may refuse to accept for filing and review any regulatory application we submit for regulatory approval in the United States. Even if our regulatory application is accepted for review, there may be delays in the FDA's review process and the FDA may determine that such regulatory application does not contain adequate clinical or other data or support the approval of the product candidate. In such a case, the FDA may issue a CRL that may require that we conduct and/or complete additional clinical trials and preclinical studies or provide additional information or data before it will reconsider our application for approval. For example, in June 2020 we received a CRL from the FDA regarding our NDA for OCA for liver fibrosis due to NASH. The CRL indicated that, based on the data the FDA had reviewed, the FDA had determined that the predicted benefit of OCA based on a surrogate

histopathologic endpoint remained uncertain and did not sufficiently outweigh the potential risks to support accelerated approval for the treatment of patients with liver fibrosis due to NASH. In addition, following the results of the New Interim Analysis, we re-submitted our NDA for OCA for pre-cirrhotic liver fibrosis due to NASH to the FDA in December 2022. There is no guarantee that the FDA will ultimately decide that any such application supports the approval of the product candidate on an accelerated basis, or at all. The FDA may also refer any regulatory application to an advisory committee for review and recommendation as to whether, and under what conditions, the application should be approved. While the FDA is not bound by the recommendation of an advisory committee, it considers such recommendations carefully when making decisions.

Even if we receive accelerated approval for any of our product candidates, we may be required to conduct or complete a post-approval clinical outcomes trial to confirm the clinical benefit of such product candidates by demonstrating the correlation of the surrogate endpoint therapeutic response in patients with a significant reduction in adverse clinical outcomes over time. For example, the results of the New Interim Analysis were based on surrogate endpoints and the impact on clinical outcomes has not been confirmed. There can be no assurance that the clinical outcomes portion of our REGENERATE trial will confirm that the surrogate endpoint used as the basis of the regulatory submissions we have made or expect to make seeking approval of OCA for liver fibrosis due to NASH will eventually show an adequate correlation with clinical outcomes.

In addition, as a condition of the accelerated approval of Ocaliva for PBC in the United States, we are required to conduct a clinical outcomes study with respect to Ocaliva for PBC. In June 2022, we announced topline results from our COBALT trial. The primary endpoint, as agreed with the FDA, was time to first occurrence of any of the following clinical endpoints: all-cause death, liver transplant, hospitalization for other serious liver-related events, signs of progression to hepatic decompensation, or signs of development of portal hypertension. The study did not demonstrate a statistically significant difference between Ocaliva and placebo on the primary endpoint. The safety and tolerability of Ocaliva were consistent with its known profile and adverse events were in line with expectations for patients with advanced PBC based on the natural history of the disease. In June 2022, we also announced topline results for our HEROES-US study, a retrospective real-world study that evaluated data from a U.S. claims database, to compare clinical outcomes in a pre-defined group of patients with PBC who were treated with Ocaliva and a comparable group of PBC patients who were eligible, but who were not treated with Ocaliva. The results from the HEROES-US study showed a statistically significant and clinically meaningful reduction in all-cause death, liver transplant, or hospitalization for hepatic decompensation among Ocaliva-treated patients compared to the control group.

In September 2022, we had an sNDA pre-submission meeting with the FDA in which we reviewed our post-marketing requirements with respect to Ocaliva. We intend to submit the data from the COBALT and HEROES-US studies as well as additional data, including data from other real world evidence studies, as part of a broader evidence package in the sNDA in support of full approval of Ocaliva for the treatment of PBC, which we anticipate submitting to the FDA in 2023. If this data package does not support fulfillment of our post-marketing obligations, we may not be able to maintain our previously granted marketing approval of Ocaliva for PBC.

Our lead development product candidate is OCA for the potential treatment of NASH. In February 2019, we announced the results of the REGENERATE Original Analysis. The REGENERATE trial is ongoing and is expected to continue through clinical outcomes for verification and description of the clinical benefit of OCA. In June 2020, we received a CRL from the FDA stating that our NDA for OCA for the treatment of liver fibrosis due to NASH could not be approved in its present form. The CRL indicated that, based on the data the FDA had reviewed, the FDA determined that the predicted benefit of OCA based on a surrogate histopathologic endpoint remained uncertain and did not sufficiently outweigh the potential risks to support accelerated approval for the treatment of patients with liver fibrosis due to NASH. We had our end of review meeting with the FDA in October 2020 to discuss the FDA's risk-benefit assessment in the CRL based on its review of the available data, as well as our proposed resubmission of our NDA for the treatment of liver fibrosis due to NASH. The meeting with FDA provided us with helpful guidance regarding supplemental data we could provide to further characterize OCA's efficacy and safety profile that could support resubmission based on our Phase 3 REGENERATE 18-month biopsy data, together with a safety assessment from our ongoing studies.

Following our end of review meeting, we had a dialogue with FDA regarding the REGENERATE study to clarify data, a new consensus read methodology for liver biopsies, and analyses required to re-submit our NDA. In connection

with the resubmission of our NDA, we conducted the New Interim Analysis. In the New Interim Analysis of the ITT population from REGENERATE, 22.4% of subjects randomized to once-daily oral OCA 25 mg met the primary endpoint of achieving at least one stage of fibrosis improvement with no worsening of NASH at month 18 on liver biopsy compared with 9.6% of subjects on placebo ($p<0.0001$). These results are consistent with the Original Analysis, which also showed that OCA 25 mg had a statistically significant effect on fibrosis improvement ($p=0.0002$). The New Interim Analysis used a consensus panel approach to histology reads, in line with recent FDA guidance, while the Original Analysis used individual central readers. A numerically greater proportion of individuals in the OCA 25 mg treatment group compared to placebo achieved the endpoint of resolution of NASH with no worsening of liver fibrosis but, consistent with the Original Analysis, the results for the endpoint of resolution of NASH were not statistically significant. As part of the New Interim Analysis, a safety evaluation was conducted in 2477 subjects from the REGENERATE trial who took at least one dose of study drug (placebo, OCA 10 mg, or OCA 25 mg). Topline results from this ongoing safety evaluation showed that treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TESAEs), and deaths were generally balanced across the OCA and placebo treatment groups in this new safety population. The most common TEAE was pruritus (24% in placebo, 33% in OCA 10 mg and 55% in OCA 25 mg) and pruritus was the most common cause for treatment discontinuation. Serious gallbladder-related events occurred in <3% of subjects in any treatment group and, consistent with its known mechanism of action, OCA 25 mg had higher rates of biliary events including gallstones.

In July 2022, we had a pre-submission meeting with the FDA in which we reviewed the planned structure and the timing of the submission of our NDA and had an ongoing dialogue as we prepared to re-submit. The Company will need to overcome the risk-benefit assessment of the FDA from the prior review of the NDA for OCA for the treatment of liver fibrosis due to NASH. Although we believe that the insights we have gained from the re-analysis and from the larger and more robust safety database provide an improved risk-benefit, there can be no assurances that the FDA will change its view on risk-benefit and will approve such NDA on an accelerated basis, or at all.

In September 2022, we announced that REVERSE, a Phase 3 study evaluating the safety and efficacy of OCA in patients with compensated cirrhosis due to NASH, did not meet its primary endpoint of a ≥ 1-stage histological improvement in fibrosis with no worsening of NASH following up to 18 months of therapy. In the REVERSE study of 919 randomized subjects with compensated cirrhosis due to NASH, 11.1% (p=NS) of subjects who were randomized to receive once-daily oral OCA 10 mg and 11.9% (p=NS) of subjects who were randomized to receive OCA 10 mg titrated to 25 mg (OCA 10-to-25 mg) after three months achieved a ≥1-stage improvement in fibrosis with no worsening of NASH after up to 18 months of treatment, compared with 9.9% of subjects who received placebo. Safety was evaluated in 916 subjects who took at least one dose of study drug (placebo, OCA 10 mg or OCA 10-to-25 mg). Treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TESAEs) and deaths were balanced across all treatment groups in REVERSE. The most common TEAE was pruritus (31% in placebo, 41% in OCA 10 mg and 57% in OCA 10-to-25 mg) and pruritus was the most common reason for treatment discontinuation. Serious gallbladder-related events were balanced across arms (0.6% in placebo, 1.0% in OCA 10 mg, 1.0% in OCA 10-to-25 mg). Consistent with the known mechanism of action of FXR-agonists, the OCA 10-to-25 mg arm had a higher incidence of gallstones.

While OCA received breakthrough therapy designation from the FDA in January 2015 for the treatment of NASH patients with liver fibrosis and we re-submitted our NDA for approval of OCA for pre-cirrhotic liver fibrosis due to NASH following the results from the New Interim Analysis in December 2022, we do not know if this will be sufficient for marketing approval or if the FDA will approve OCA for liver fibrosis due to NASH on an accelerated or conditional basis, or at all. There may be delays in the FDA review processes and the FDA may also require that we continue our Phase 3 REGENERATE trial until completion to assess the potential benefits of OCA treatment on liver-related and other clinical outcomes for purposes of marketing approval. Our regulatory pathway for OCA for the treatment of NASH will depend upon our ongoing discussions with the FDA. As a result, we may face difficulty in establishing an acceptable registration strategy with respect to our Phase 3 REGENERATE trial, as well as other trials we may conduct in other subpopulations of NASH patients.

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

Delays or difficulties in the commencement, enrollment and completion of our clinical trials and studies could increase our product development costs and limit or prevent us from obtaining or maintaining regulatory approval for OCA and our other product candidates. The results of our clinical trials may not be available when we anticipate and we may be required to conduct additional clinical trials or studies not currently planned in order for our product candidates, including OCA for PBC and NASH, to be approved or to maintain approvals in the U.S. In addition, our clinical programs are subject to a number of risks and uncertainties, such as the results of other trials, patient enrollment, safety issues or regulatory interactions that could result in a change of trial design or timing. Any delays or difficulties in completing one of our clinical trials could increase our product development costs and limit or prevent us from obtaining or maintaining regulatory approval. Consequently, we do not know whether our current or future clinical trials or studies of OCA or our other product candidates will be completed on schedule, if at all.

For example, our Phase 3 REGENERATE trial is a large and complicated clinical trial in a disease without any approved therapies and involves serial liver biopsies over many years. While we announced the topline results from the New Interim Analysis in July 2022, there can be no assurance the FDA will approve our NDA for OCA for NASH on an accelerated or conditional basis, or at all. In September 2022, we announced that our REVERSE trial evaluating the safety and efficacy of OCA in patients with compensated cirrhosis due to NASH, did not meet its primary endpoint of a ≥ 1-stage histological improvement in fibrosis with no worsening of NASH following up to 18 months of therapy. As we engage in other large and complicated trials and trials in advanced disease populations, we may experience a number of challenges that may negatively affect or delay our plans and development programs.

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

Clinical failure can occur at any stage of clinical development. Clinical trials may produce negative or inconclusive results, and we or our collaborators may decide, or regulators may require us, to conduct additional clinical trials or preclinical studies. In addition, data obtained from trials and studies are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may delay, limit or prevent regulatory approval. Success in preclinical studies and early clinical trials does not ensure that subsequent clinical trials will generate the same or similar results or otherwise provide adequate data to demonstrate the efficacy and safety of our product candidates. A number of companies in the pharmaceutical industry, including those with greater resources and experience than us, have suffered significant setbacks in Phase 3 clinical trials and at other stages of clinical development, even after seeing promising results in earlier clinical trials. For example, in September 2022, we announced that our REVERSE trial did not meet its primary endpoint of a ≥ 1-stage histological improvement in fibrosis with no worsening of NASH following up to 18 months of therapy.

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

There may be significant variability in the safety and/or efficacy results we see in different trials studying OCA or our other product candidates due to numerous factors, including differences in the underlying disease being studied, changes or differences in trial protocols or statistical analysis plans, differences in the composition of the patient populations or clinical trial sites, differences in adherence to the dosing regimen and other aspects of the trial protocols and differences in the rate of dropouts among clinical trial participants. We do not know whether any Phase 2, Phase 3 or other clinical trials we or any of our collaborators may conduct on our product candidates will demonstrate consistent or adequate

efficacy and safety or result in the approval of our product candidates by regulatory authorities. If we are unable to bring any of our current or future product candidates to market, acquire any previously approved products or maintain approval for our approved products, our ability to create long-term stockholder value will be limited.

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

In February 2019, we announced the results from the REGENERATE Original Analysis. In the primary efficacy analysis, once-daily OCA 25 mg met, with statistical significance, the primary endpoint agreed with the FDA of fibrosis improvement by at least one stage with no worsening of NASH (defined as no worsening of hepatocellular ballooning, no worsening of lobular inflammation and no worsening of steatosis) at the planned 18-month analysis. Although a numerically greater proportion of patients in both OCA treatment groups compared to placebo achieved the primary endpoint of NASH resolution with no worsening of liver fibrosis in the primary efficacy analysis, this result did not reach statistical significance. As agreed with the FDA, in order for the primary objective to be met, the study was required to achieve one of the two primary endpoints. Notwithstanding the results of the REGENERATE 18-month analysis, the CRL indicated that, based on the data the FDA had reviewed, the FDA had determined that the predicted benefit of OCA based on a surrogate histopathologic endpoint remained uncertain and did not sufficiently outweigh the potential risks to support accelerated approval for the treatment of patients with liver fibrosis due to NASH. The FDA recommended that we submit additional post-interim analysis efficacy and safety data from the ongoing REGENERATE study in support of potential accelerated approval and that the long-term outcomes phase of the study should continue.

In connection with the resubmission of our NDA, we conducted a new interim analysis of our ongoing pivotal Phase 3 REGENERATE trial of OCA using a biopsy consensus read methodology in the same ITT population as the Original Analysis. In July 2022, we announced topline results from our New Interim Analysis. In this new interim analysis of the ITT population from REGENERATE, once-daily OCA 25 mg met, with statistical significance, the primary endpoint agreed with the FDA of fibrosis improvement by at least one stage with no worsening of NASH at month 18. The New Interim Analysis used a consensus panel approach to histology reads, in line with recent FDA guidance, while the Original Analysis used individual central readers. A numerically greater proportion of individuals in the OCA 25 mg treatment group compared to placebo achieved the endpoint of resolution of NASH with no worsening of liver fibrosis but, consistent with the Original Analysis, the results for the endpoint of resolution of NASH were not statistically significant. As part of the New Interim Analysis, a safety evaluation was conducted in 2477 subjects from the REGENERATE trial who took at least one dose of study drug (placebo, OCA 10 mg, or OCA 25 mg). Topline results from this ongoing safety evaluation showed that treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TESAEs), and deaths were generally balanced across the OCA and placebo treatment groups in this new safety population. The most common TEAE was pruritus (24% in placebo, 33% in OCA 10 mg and 55% in OCA 25 mg) and pruritus was the most common cause for treatment discontinuation. Serious gallbladder-related events occurred in <3% of subjects in any treatment group and, consistent with its known mechanism of action, OCA 25 mg had higher rates of biliary events including gallstones.

In September 2022, we announced that REVERSE, a Phase 3 study evaluating the safety and efficacy of OCA in patients with compensated cirrhosis due to NASH, did not meet its primary endpoint of a ≥ 1-stage histological improvement in fibrosis with no worsening of NASH following up to 18 months of therapy. In the REVERSE study of 919 randomized subjects with compensated cirrhosis due to NASH, 11.1% (p=NS) of subjects who were randomized to receive once-daily oral OCA 10 mg and 11.9% (p=NS) of subjects who were randomized to receive OCA 10 mg titrated to 25 mg (OCA 10-to-25 mg) after three months achieved a ≥1-stage improvement in fibrosis with no worsening of NASH after up to 18 months of treatment, compared with 9.9% of subjects who received placebo.

Although we re-submitted our NDA for approval of OCA for pre-cirrhotic liver fibrosis due to NASH following the results of the New Interim Analysis to the FDA in December 2022, we do not know if such results will be sufficient for marketing approval or if the FDA will approve OCA for liver fibrosis due to NASH on an accelerated or conditional basis, or at all.

In connection with Ocaliva's accelerated approval in the United States and conditional approval in the European Union, we committed to conduct a Phase 4 confirmatory outcomes trial of Ocaliva, known as the COBALT trial, and other clinical trials to satisfy post-marketing regulatory requirements. Continued approval of Ocaliva for PBC is contingent upon the verification and description of clinical benefit in the COBALT trial and our satisfaction of our other post-marketing regulatory requirements. Further, as part of our post-marketing requirements for Ocaliva, we undertook a Phase 4 clinical trial of Ocaliva in patients with PBC who have moderate to severe hepatic impairment (Child-Pugh B and C) (known as the 401 trial).

Changes to our Ocaliva label with respect to patients with PBC with decompensated cirrhosis (e.g., Child-Pugh Class B or C), a prior decompensation event, or compensated cirrhosis with evidence of portal hypertension influenced modifications to our COBALT study design, and, as a result of the changes to the U.S. prescribing information, we also removed from the trial subjects in the United States who are now excluded from the scope of the label. We also agreed with the FDA and the EMA to terminate our 401 trial, in light of the exclusion of patients with PBC with decompensated cirrhosis from the Ocaliva label in the U.S. In addition, a DMC reviewed the unblinded results of a pre-specified interim efficacy analysis of the COBALT trial and separately reviewed unblinded safety and pharmacokinetic data from both the COBALT and 401 trials. Following these reviews, the DMC stated that it was not feasible to continue the COBALT trial as designed and noted the challenges in enrolling and maintaining placebo-controlled post-marketing studies in this rare disease setting. Given the feasibility concerns noted by the DMC as well as the potential confounding impact of subjects discontinuing treatment and/or transitioning from investigational product to commercial drug during clinical trials, we discussed with the FDA and the EMA proposed modifications to the COBALT trial, and we notified the FDA and the EMA of the DMC's recommendation. Based on discussions with both the FDA and the EMA, we closed our COBALT and 401 trials and compiled data available from these studies.

In June 2022, we announced topline results from our COBALT trial. The primary endpoint, as agreed with the FDA, was time to first occurrence of any of the following clinical endpoints: all-cause death, liver transplant, hospitalization for other serious liver-related events, signs of progression to hepatic decompensation, or signs of development of portal hypertension. The study did not demonstrate a statistically significant difference between Ocaliva and placebo on the primary endpoint. The safety and tolerability of Ocaliva were consistent with its known profile and adverse events were in line with expectations for patients with advanced PBC based on the natural history of the disease. In June 2022, we also announced topline results for our HEROES-US study, a retrospective real-world study that evaluated data from a U.S. claims database, to compare clinical outcomes in a pre-defined group of patients with PBC who were treated with Ocaliva and a comparable group of PBC patients who were eligible, but who were not treated with Ocaliva. The results from the HEROES-US study showed a statistically significant and clinically meaningful reduction in all-cause death, liver transplant, or hospitalization for hepatic decompensation among Ocaliva-treated patients compared to the control group.

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

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

The most common side effects observed in clinical trials of OCA for PBC were pruritus, fatigue, headaches, nausea, constipation and diarrhea. In our Phase 3 POISE trial, pruritus, generally mild to moderate, was the most frequently reported adverse event associated with OCA treatment for PBC and was observed in 38% of patients on placebo, 70% of patients in the OCA 10 mg group and 56% of patients in the OCA titration group (5 mg to 10 mg). Eight patients discontinued due to pruritus, of whom none were in the placebo group, seven (10%) were in the OCA 10 mg group and one (1%) was in the OCA titration group. Pruritus also has been observed in other clinical trials of OCA. Decreases in high density lipoprotein HDL cholesterol were also observed during treatment in our Phase 3 POISE trial. In our Phase 2 trials for OCA for PBC, a dose-response relationship was observed in the occurrence of liver-related adverse reactions, including jaundice, ascites and primary biliary cholangitis flare with dosages of OCA of 10 mg once daily to 50 mg once daily (up to 5-times the highest recommended dosage), as early as one month after starting treatment with OCA.

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

In 2020 the FDA notified us that, in the course of its routine safety surveillance, in May of that year it began to evaluate a newly identified safety signal, or NISS, regarding liver disorder for Ocaliva which the FDA classified as a potential risk, focused on a subset of the cirrhotic, or more advanced, PBC patients who had taken Ocaliva. In May 2021, the NISS process was concluded and we aligned with the FDA on updated Ocaliva prescribing information in the United States, and Ocaliva is now contraindicated for patients with PBC and decompensated cirrhosis, a prior decompensation event, or compensated cirrhosis with evidence of portal hypertension, in addition to the existing contraindication for complete biliary obstruction. This issue, and any other safety concerns associated with Ocaliva, perceived or real, may adversely affect the successful development and commercialization of our product candidates and approved products, including Ocaliva, and materially and adversely affect our business including future revenue generated by Ocaliva.

In June 2022, we announced the results of our COBALT study. The safety and tolerability of Ocaliva were consistent with its known profile and adverse events were in line with expectations for patients with advanced PBC based on the natural history of the disease.

In July 2022, we announced topline safety results from the New Interim Analysis of our REGENERATE study. Compared to the Original Analysis, the safety population in the New Interim Analysis had significantly longer exposure to study drug (median 42 months vs. 15 months), yielding more than 8,000 total patient-years and 3.4 times more exposure. As part of the New Interim Analysis, a safety evaluation was conducted in 2477 subjects from the REGENERATE trial who took at least one dose of study drug (placebo, OCA 10 mg, or OCA 25 mg). Topline results from this ongoing safety evaluation showed that treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TESAEs), and deaths were generally balanced across the OCA and placebo treatment groups in this new safety population. The most common TEAE was pruritus (24% in placebo, 33% in OCA 10 mg and 55% in OCA 25 mg) and pruritus was the most common cause for treatment discontinuation. Serious gallbladder-related events occurred in <3% of subjects in any treatment group and, consistent with its known mechanism of action, OCA 25 mg had higher rates of biliary events

including gallstones. As part of the safety review of the New Interim Analysis, independent groups of experts reviewed certain categories of safety events to provide a blinded adjudication as specifically requested by the FDA. These included events pertaining to hepatic (excluding clinical outcomes), cardiovascular and renal safety. Topline analysis through four years of treatment showed a numerically higher number of adjudicated hepatic safety events for OCA 25 mg, the majority of which were mild in severity. For adjudicated core major adverse cardiovascular events and adjudicated acute kidney injury events, frequency of events was low and balanced across treatment groups. Consistent with its mechanism of action as an FXR agonist, OCA treatment was associated with an increase in LDL at Month 1 which returned to near baseline values by Month 12.

In September 2022, we announced topline results for REVERSE, a Phase 3 study evaluating the safety and efficacy of OCA in patients with compensated cirrhosis due to NASH. Safety was evaluated in 916 subjects who took at least one dose of study drug (placebo, OCA 10 mg or OCA 10-to-25 mg). Treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TESAEs) and deaths were balanced across all treatment groups in REVERSE. The most common TEAE was pruritus (31% in placebo, 41% in OCA 10 mg and 57% in OCA 10-to-25 mg) and pruritus was the most common reason for treatment discontinuation. Serious gallbladder-related events were balanced across arms (0.6% in placebo, 1.0% in OCA 10 mg, 1.0% in OCA 10-to-25 mg). Consistent with the known mechanism of action of FXR-agonists, the OCA 10-to-25 mg arm had a higher incidence of gallstones.

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

In our CONTROL trial, dose-dependent pruritus was the most common adverse event in patients treated with OCA, occurring in 5% of patients on placebo, 5% of patients in the OCA 5 mg group, 10% of patients in the OCA 10 mg group and 55% of patients in the OCA 25 mg group. All adverse events were mild to moderate, and two patients discontinued treatment in the OCA 25 mg group due to pruritus. Over 95% of the patients completing the double-blind phase of CONTROL enrolled in the LTSE phase of the trial. During the LTSE phase of CONTROL, there was one patient death, which the principal investigator determined was unlikely related to OCA.

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

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

In addition, our product candidates are being developed as potential treatments for severe, life-threatening diseases and, as a result, our trials will necessarily be conducted in patient populations that are more prone than the general population to exhibit certain disease states or adverse events. Ocaliva is prescribed in patients suffering from various stages of PBC, which can be life threatening, and patients may suffer from other concomitant illnesses that may increase the likelihood of certain adverse events. It may be difficult to discern whether certain events or symptoms observed during our clinical trials or by patients using our approved products are related to our product candidates or approved products or

some other factor. As a result, we and our development programs may be negatively affected even if such events or symptoms are ultimately determined to be unlikely related to our product candidates or approved products. We cannot assure you that additional or more severe adverse side effects related to OCA or our other product candidates will not be observed in our clinical trials or in the commercial setting. If observed, such adverse side effects could delay or preclude regulatory approval of OCA, limit commercial use or result in the withdrawal of previously granted marketing approvals.

Continuing threats from COVID-19, including additional waves of infections, could materially and adversely affect our clinical trials.

COVID-19 is a global pandemic, affecting the U.S., Europe, and other countries in which we are engaged in, or plan to engage in, clinical development activities. We continue to closely monitor the latest developments regarding the COVID-19 pandemic and, together with our contract research organizations, study sites and other partners, have taken measures intended to minimize disruptions and protect and retain patients enrolled in our clinical trials, including, where appropriate, the use of telemedicine, home care visits, direct delivery of investigational product and other measures. Notwithstanding our efforts, some of the sites participating in our clinical trials have been affected by site closings or reduced capacity, particularly in regions that are experiencing heightened impact from COVID-19. While we continue to monitor the latest developments regarding the COVID-19 pandemic closely, if there was a meaningful negative impact on the data capture or data quality of any of our clinical trials, such trials may not be successful or we could be required to repeat, extend the duration of, increase the size of, or otherwise modify such trials, which could prevent or significantly delay the potential commercialization of our product candidates and require greater expenditures. We cannot at this time predict with certainty the scope of the impact of COVID-19 on our ability to execute our clinical trials. We may experience issues due to COVID-19 that could severely impact our clinical trials, including:

- delays, interruptions or difficulties in the enrollment, scheduling and retention of patients in our clinical trials;
- delays, interruptions or difficulties in the conduct of key clinical trial activities, such as clinical trial site monitoring and inspection readiness activities;
- trial conduct issues, including protocol deviations (e.g., failure to timely collect liver biopsies or other required laboratory data), data capture issues and data quality issues;
- delays or interruptions in the supply or administration of investigational product to patients in our clinical trials;
- delays or interruptions in the supply of necessary equipment or materials to clinical sites;
- delays or difficulties obtaining approvals from regulatory authorities, institutional review boards or ethics committees of clinical trial protocols and related clinical documentation (or amendments and addendums thereto);
- delays, interruptions or difficulties in clinical site initiations, including in connection with the recruitment of clinical site investigators and clinical site staff;
- the redeployment of healthcare resources, including clinical site investigators and clinical site staff supporting the conduct of our clinical trials, to assist in the treatment of COVID-19 patients;
- the diversion of human capital, including employees, independent contractors, vendors and other third parties, otherwise focused on the conduct of our clinical trials due to sickness, safety concerns or government or employer imposed travel or working restrictions;

- new federal, state and local government regulations or guidance that require us to change the way we conduct our clinical trials, require the interruption or termination of our clinical trials or that result in significant and unexpected new costs;

- delays or difficulties in interactions with regulatory authorities, institutional review boards, ethics committees and key consultants and vendors due to layoffs, temporary leaves, terminations or other actions limiting available employee resources; and

- the refusal of regulatory authorities to accept clinical trial data from clinical trials that have been negatively affected by COVID-19.

Any such delay, interruption or issue could materially and adversely affect our business, financial condition and results of operations.

Risks Related to Our Financial Position and Need for Additional Capital

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

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

Our ability to generate profits from operations and become profitable currently depends on the commercial success of Ocaliva for PBC. However, the successful commercialization of Ocaliva for PBC is subject to many risks, and there is no guarantee that we will be able to continue to commercialize Ocaliva successfully. There are numerous examples of unsuccessful commercial efforts, as well as failures to meet expectations of market potential, including by pharmaceutical companies with greater experience and resources than us.

The commercial success of Ocaliva for PBC depends on the extent to which patients, physicians and payers accept and adopt Ocaliva as a treatment for PBC, and we do not know whether our or others' estimates in this regard will be accurate. As such, there is significant uncertainty in the degree of market acceptance that Ocaliva will have for PBC. For example, if the patient population suffering from PBC is smaller than we estimate, or even if the patient population matches our estimates but Ocaliva is not widely accepted as a treatment for PBC, the commercial potential of Ocaliva for PBC will be limited. Physicians may not prescribe Ocaliva and patients may be unwilling to use Ocaliva if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost. Additionally, the use of Ocaliva in a non-trial setting may result in the occurrence of unexpected or a greater incidence of side effects, adverse reactions or misuse that may negatively affect the commercial prospects of Ocaliva for PBC.

Furthermore, any negative development in any other development program for OCA or our failure to satisfy the post-marketing regulatory commitments and requirements to which we are or may become subject, including any study to assess the clinical benefit of Ocaliva in PBC may materially and adversely impact the commercial results and potential of Ocaliva for PBC. For example, in June 2022, we announced topline results from our COBALT trial, which did not demonstrate a statistically significant difference between Ocaliva and placebo on the primary endpoint. While we intend to submit the data from the COBALT study as well as additional data, including data from other real world evidence studies, as part of a broader evidence package in support of full approval of Ocaliva for the treatment of PBC, if this data package does not support fulfillment of our post-marketing obligations, we may not be able to maintain our previously granted marketing approval of Ocaliva for PBC.

In May 2021, we updated the Ocaliva prescribing information in the United States and Ocaliva is now contraindicated for patients with PBC and decompensated cirrhosis, a prior decompensation event, or compensated cirrhosis with evidence

of portal hypertension, in addition to the existing contraindication for complete biliary obstruction. Corresponding limitations on the use of Ocaliva in our potential patient population, or similar safety concerns, could reduce our sales.

As a result, it is uncertain whether Ocaliva net sales for PBC will sustain our operations and it may take a significant amount of time before Ocaliva net sales for PBC sustain our operations. If the commercialization of Ocaliva for PBC is unsuccessful or perceived to be unsuccessful, the long-term prospects of Ocaliva for PBC, as well as the long-term prospects of our company, may be materially and adversely affected.

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

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

Our continuing operations have never been profitable and we do not expect them to be profitable in the foreseeable future. We incurred net losses from continuing operations of $174.9 million, $136.4 million and $273.4 million for the years ended December 31, 2022, 2021 and 2020, respectively. To date, we have financed our operations primarily through public offerings and private placements of our securities, sales of product and payments received under licensing and collaboration agreements, including pursuant to our sale of our ex-U.S. commercial business to Advanz and related sublicense. At December 31, 2022, we had $490.9 million in cash, cash equivalents, restricted cash and investment debt securities.

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

We expect to continue to incur losses for the foreseeable future, and we expect these losses to be significant as we, among other things, develop and seek regulatory approval for our product candidates, including OCA for liver fibrosis due to NASH, maintain our regulatory approvals and commercialize our approved products. We believe our prospects and ability to significantly grow revenues will be dependent on our ability to successfully develop and commercialize OCA for indications other than PBC, such as NASH, and to identify strategic business development opportunities to leverage our capabilities in rare diseases. As a result, we expect a significant amount of resources to continue to be devoted to our development programs for OCA and to developing our pipeline.

As part of our product development activities, we currently expect to continue our Phase 3 clinical program of OCA for liver fibrosis due to NASH, including our Phase 3 REGENERATE trial in patients with liver fibrosis due to NASH through clinical outcomes for verification and description of clinical benefit. Our expenses could increase if we are required by regulators to perform studies or trials in addition to those currently expected, if our current trials are modified for any reason, or if there are any issues or delays in completing our clinical trials or the development of any of our product candidates, due to COVID 19 or otherwise. For example, in June 2020 we received a CRL from the FDA with respect to our NDA for OCA for liver fibrosis due to NASH. The CRL indicated that, based on the data the FDA had reviewed, the FDA has determined that the predicted benefit of OCA based on a surrogate histopathologic endpoint remains uncertain and does not sufficiently outweigh the potential risks to support accelerated approval for the treatment of patients with liver fibrosis due to NASH. The FDA recommended that we submit additional post-interim analysis efficacy and safety data from the ongoing REGENERATE trial in support of potential accelerated approval and that the long-term outcomes phase of the trial should continue. Although we re-submitted our NDA seeking accelerated approval of OCA for the

treatment of pre-cirrhotic liver fibrosis due to NASH to the FDA in December 2022, there is no assurance that we will be successful or that OCA will be approved for pre-cirrhotic liver fibrosis due to NASH on an accelerated basis, or at all. Accordingly, our previously anticipated U.S. commercial launch of OCA for liver fibrosis due to NASH prior to receipt of the CRL was postponed, we do not expect to generate revenues for this indication until it has been approved, and we may incur significantly greater costs than previously anticipated in connection with the development of OCA for liver fibrosis due to NASH.

We intend to continue to develop OCA and our other existing product candidates, alone or in combination, for non-viral liver diseases. If OCA or any of our other product candidates fails in clinical trials or does not gain or maintain regulatory approval, or if OCA or any of our other product candidates does not achieve market acceptance, we may never become profitable. Our net losses and, when applicable, negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. Because of the numerous risks and uncertainties associated with pharmaceutical product development and commercialization, we are unable to predict with certainty the timing or amount of our expenses, whether such expenses may increase, or when, or if, we will be able to achieve profitability. The amount of our future net losses will depend, in part, on our future expenses, whether and by how much such expenses increase and our ability to generate revenues.

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

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

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

As of December 31, 2022, we had $490.9 million in cash, cash equivalents, restricted cash and investment debt securities. We expect to continue to incur significant operating expenses in the fiscal year ending December 31, 2023. These expenses are planned to support, among other initiatives, the continued commercialization of Ocaliva for PBC, our continued clinical development of OCA for PBC and NASH and our other earlier stage research and development programs. Although we believe that our existing capital resources, together with our net sales of Ocaliva for PBC, will be sufficient to fund our anticipated operating requirements for the next twelve months, we may need to raise additional capital to fund our operating requirements beyond that period. Furthermore, in light of our receipt in June 2020 of a CRL from the FDA with respect to our NDA for OCA for liver fibrosis due to NASH and the numerous risks and uncertainties associated with pharmaceutical product development and commercialization, any delays in, or unanticipated costs associated with, our development, regulatory or commercialization efforts could significantly increase the amount of capital required by us to fund our operating requirements. Accordingly, we may seek to access the public or private capital markets whenever conditions are favorable, even if we do not have an immediate need for additional capital at that time.

Our forecasts regarding the period of time that our existing capital resources will be sufficient to meet our operating requirements and the timing of our future funding requirements, both near and long-term, will depend on a variety of

factors, many of which are outside of our control. Such factors include, but are not limited to, those factors listed above under "Cautionary Note Regarding Forward-Looking Statements".

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

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

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

The terms of any future financing may adversely affect the interests of our existing securityholders. For example, to the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, in addition to covenants under our existing debt financings. We also could be required to seek funds through arrangements with licensing or collaborative partners or otherwise that may require us to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to the Transaction with Advanz

We or Advanz may fail to perform under any of the agreements entered into in connection with the Advanz transaction, we may be subject to incremental costs related to our ongoing relationship with Advanz, and we may fail to receive certain financial benefits from the transaction. As a result, our business may be adversely affected.

On July 1, 2022, we completed the sale of our ex-U.S. commercial operations to Advanz, and sublicensed the right to commercialize Ocaliva and OCA for NASH outside of the United States. Our transaction with Advanz is subject to risks, that we may not be able to control and therefore our business may be adversely affected.

- Under the SMA, OCA will be supplied in bulk tablet form. If we encounter supply chain delays or are unable to procure sufficient supplies of OCA, we may not be able to fulfill our supply obligations to Advanz under the SMA, and this could also impact the fulfillment of our own supply needs for OCA.

- If Advanz breaches the contractual obligations owed to us pursuant to the SMA, the Sublicense Agreement or the other transactions documents, we could be exposed to commercial, regulatory or other liabilities.

- We may be subject to incremental costs in connection with ongoing studies with respect to Ocaliva for PBC and other development activities related thereto, including with respect the studies we will continue to support under our agreements with Advanz.

- We may not be able to adequately protect our intellectual property or become involved in intellectual property enforcement actions, which may cause us to incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights, and such litigation may divert the attention of our management and scientific personnel and adversely affect our development and commercialization efforts.

- We may not be able to detect and prevent fraud, breaches of regulations, anticorruption and laws and other misconduct by Advanz or our former employees, which could expose us to liability.

- Our ability to receive certain economic benefits from the transaction, including the earnout and royalties from the commercial sale of OCA for NASH outside of the U.S., is dependent upon certain contingencies which are beyond our control, including the extension of pediatric orphan exclusivity in Europe for Ocaliva and marketing approval of OCA for NASH in markets outside of the United States. As a result, we may not receive certain economic benefits from the Advanz transaction.

Any of these factors could cause us to incur higher costs, disrupt the supply of our product candidates or approved products, delay the approval of our product candidates or prevent or disrupt the commercialization of our approved products.

Risks Related to Our Business and Strategy

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

We outsource and plan to continue to outsource substantial portions of our operations to third-party service providers, including CROs for certain of our clinical trial and product development activities, and contract manufacturers for the production of API and finished drug product for our commercial sales, clinical trials and preclinical studies. We will likely also use the services of third-party vendors in connection with our future commercialization activities, including product sales, marketing and distribution. Our agreements with third-party service providers are typically on a study-by-study and/or project-by-project basis. Typically, we may terminate these agreements with notice and are responsible for the supplier's previously incurred costs. In addition, a number of third-party service providers that we retain will be subject to the FDA's and EMA's regulatory requirements and similar standards outside of the United States and Europe and we do not have control over compliance with these regulations by these providers. If these providers do not adhere to applicable governing practices and standards, the commercialization of Ocaliva and our other approved products, if any, and the development of OCA 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. Outsourcing these functions involves the risk that third parties may not perform to our standards, may not produce results in a timely manner or may fail to perform at all. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated. There are a limited number of third-party service providers that have the specialized expertise required to achieve our business objectives. Identifying, qualifying and managing the performance of third-party service providers can be difficult, time-consuming and cause delays in our development programs. Despite our growth, we have limited internal resources available to identify and monitor third-party service providers. To the extent we are unable to identify, retain and successfully manage the performance of third-party service providers, our business may be materially and adversely affected. We may further be subject to the imposition of civil or criminal penalties if our third party service providers violate applicable law.

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

The effects of COVID-19 and related public health safety measures and business closures and disruptions may negatively impact our and our third-party service providers' productivity, limit the conduct of business operations and impair our and our third-party service providers' ability to conduct operations.

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

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We have competitors in the United States, Europe and other jurisdictions, including major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical and generic drug companies and universities and other research institutions. Many of our competitors have financial, sales and marketing, manufacturing and distribution, legal, regulatory and product development resources substantially greater than ours. Large pharmaceutical companies, in particular, have extensive experience in research, clinical testing, obtaining regulatory approvals, recruiting patients and manufacturing pharmaceutical products. These companies also have significantly greater sales and marketing capabilities and often have collaborative arrangements in our target markets. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make our products or product candidates obsolete. As a result of all of these factors, our competitors may succeed in obtaining patent protection and/or FDA, EMA or other regulatory approval or discovering, developing and commercializing drugs for the diseases that we are targeting before we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. See "Item 1. Business—Our Product Candidates—Competition", particularly for discussion of Madrigal Pharmaceuticals, Inc. and other potential competitors of ours in treating PBC or liver fibrosis due to NASH.

Additionally, competition from generic manufacturers could hinder commercialization efforts of our products. For example, we received paragraph IV certification notice letters from seven generic drug manufacturers indicating that each such company had submitted to the FDA an ANDA seeking approval to manufacture and sell a generic version of our 5 mg and 10 mg dosage strengths of Ocaliva® (obeticholic acid) for PBC prior to the expiration of certain patents listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book") for Ocaliva (the "Ocaliva Patents"). The paragraph IV certification notices each allege that the Ocaliva Patents are invalid, unenforceable, and/or will not be infringed by the manufacture, use or sale of the generic medicine for which the ANDA was submitted. We timely initiated patent infringement suits against each of these generic drug manufacturers in the United States District Court for the District of Delaware seeking injunctions to prevent each generic drug manufacturer from selling a generic version of Ocaliva prior to the expiration of the Ocaliva Patents. The Company has settled with six of the seven generic drug manufacturers involved. We intend to vigorously defend and enforce our intellectual property rights protecting Ocaliva against the remaining generic manufacturer. We note, however, that such patent litigations are costly and time-consuming, and we can offer no assurance as to when the remaining lawsuit will be decided, or whether the lawsuit will be successful. If a generic equivalent of Ocaliva is approved and enters the market before the expiration of the Ocaliva Patents without license from the Company, our business may be materially and adversely affected. See Note 16 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for more information.

Off-label uses of other potential treatments may also limit the commercial potential of our products and product candidates, especially given the pricing of Ocaliva and the anticipated pricing for our product candidates. For example, while fibrates are not approved for use in PBC, off-label use of fibrate drugs has been reported. In NASH, a number of treatments are used off-label (see the "Business-Competition" section above).

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

- the results of our and our strategic collaborators' clinical trials and preclinical studies;
- our ability to recruit, enroll and retain patients for our clinical trials;
- the efficacy, safety and tolerability of Ocaliva, OCA for liver fibrosis due to NASH, if approved, and our other future approved products, if any;

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

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

Our business and operations would suffer in the event of system failures or security or data breaches due to cyber-attacks, or cyber intrusions, including ransomware, phishing attacks and other malicious intrusions.

In recent years, cybersecurity threats have become a greater risk and focus for companies. In particular, ransomware attacks, where a hacker locks and threatens to delete or disclose the victim's data unless a ransom is paid, has become a major risk. We and our third-party service providers are at risk of cyber-attacks or cyber intrusions via the Internet, computer viruses, break-ins, malware, ransomware, phishing attacks, hacking, denial-of-service attacks or other attacks and similar disruptions from the unauthorized use of, or access to, computer systems (including from internal and external sources). These types of incidents continue to be prevalent and pervasive across industries, including in our industry. In addition, we expect information security risks to continue to increase due to the proliferation of new technologies and the increased sophistication and activities of organized crime, hackers, terrorists and other external parties, including foreign state actors.

We are increasingly dependent on information technology systems and infrastructure, including mobile technologies, to operate our business. In the ordinary course of our business, we collect, process, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such information. The size and complexity of our information technology systems, and those of third-party vendors with whom we contract, and the volume of data we retain, make such systems potentially vulnerable to breakdown, malicious intrusion, security breaches, ransomware, phishing, and other cyber-attacks. Our information security systems and those of our third-party vendors are subject to laws and regulations, or may become subject to new laws and regulations, requiring that we enact certain measures to protect the privacy and security of certain information we collect or use in our business. A security breach or privacy violation that leads to disclosure or modification of, or prevents access to, personal information or other protected

information, whether caused by internal or external parties, could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to notification requirements under certain agreements with third parties, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to liability under laws and regulations that protect personal information, resulting in increased costs or loss of revenue. Similarly, the loss or unauthorized disclosure of clinical trial data from completed, ongoing or planned clinical trials could prevent us from obtaining regulatory approval or delay our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

If we are unable to prevent such security breaches or privacy violations or implement satisfactory remedial measures, our operations could be disrupted, and we may suffer negative impact to our reputation, financial loss and be subject to regulatory fines and penalties. In addition, breaches and other unauthorized data access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. Moreover, the reliance on remote working technologies by our employees and third-party partners due to COVID-19 and related public health safety measures and the prevalent use of mobile devices that access confidential and personal information increases the risk of data security breaches, which could lead to the loss of confidential information, personal information, trade secrets or other intellectual property. As cyber threats continue to evolve, we may be required to expend significant additional resources to continue to modify or enhance our protective measures or to investigate and remediate any information security vulnerabilities. While we have implemented security measures to protect our data security and information technology systems, such measures may not prevent such events. Significant disruptions of our information technology systems or breaches of data security could have a material adverse effect on our business, financial condition and results of operations.

We are subject to various data protection laws and our business and operations would suffer in the event of violations of these laws.

In the United States, numerous federal and state laws, including, without limitation, HIPAA, 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 as well as consumer rights with regard to such information. For example, California passed the California Consumer Privacy Act of 2018, which became effective on January 1, 2020, and the California Privacy Rights Act became effective in January 2023 and enforceable in July 2023, giving California consumers further privacy rights, largely aligned with EU privacy rights. Other states, including Virginia, Colorado, Connecticut and Utah have enacted similar privacy laws. Various foreign countries where we may process personal information also have, or are developing, privacy and data protection laws governing the collection, use, disclosure and storage of personal information.

In May 2018, the General Data Protection Regulation (the "GDPR") took effect in the European Economic Area (the "EEA"). The GDPR imposes more stringent data protection requirements, and provides for greater penalties for noncompliance, than previous EEA data protection legislation. In addition, although we have implemented certain measures as a result of Brexit to allow for the transfer of personal data between EEA member states and the United Kingdom, we may need to develop additional mechanisms to permit for the transfer of this data. Implementation of the GDPR and other changes in privacy and data protection laws or regulations could require changes to certain of our business practices, thereby increasing our costs. While we continue to engage in activities to comply with the GDPR requirements and other data protection laws, we may be unsuccessful in these efforts.

Since 2016, Intercept has been certified to the EU-U.S. Privacy Shield and the Swiss-U.S. Privacy Shield, which provided a framework that the EU Commission considered to provide an adequate level of data protection of personal data of EU (and Swiss) residents. On July 16, 2020, the Court of Justice of the European Union ("CJEU") invalidated the EU-U.S. Privacy Shield as a data transfer mechanism for transferring personal data from the EEA to the United States, effective immediately. On September 20, 2020, the Swiss Federal Data Protection and Information Commissioner invalidated the Swiss-U.S. Privacy Shield. Therefore, the EU-U.S. Privacy Shield and the Swiss-U.S. Privacy Shield no longer qualify as appropriate safeguards for the transfer of personal data from the EEA or Switzerland to the United States. While the European Commission approved Standard Contractual Clauses ("SCCs") and Binding Corporate Rules remain valid mechanisms to transfer personal data to third countries outside the EEA and Switzerland, the CJEU's ruling has also imposed enhanced due diligence obligations on organizations acting as data exporters and relying on SCCs to ensure that the laws of the country to which personal data is transferred offers a level of data protection that is essentially equivalent

to the EEA. On June 4, 2021, the European Commission adopted new SCCs more aligned with the requirements of the GDPR and to be used when personal data is transferred outside of the European Union. On June 28, 2022, the EU Commission granted "adequacy" to the UK, allowing the free flow of EU resident personal data from the EU to recipients located in the UK. However, due to the UK's withdrawal from the EU, the new SCCs are not valid for transfers of UK resident personal data to countries outside of the UK. The UK Information Commissioner's Office has issued its International Data Transfer Agreement ("IDTA") to facilitate such transfers. Accordingly, contracts have been, or are in the process of being, updated with the new UK IDTAs, as applicable. To the extent that we are not able to employ suitable data transfer mechanisms, including the implementation of the new SCCs and IDTAs, to facilitate international transfers of data, our ability to conduct our business may be materially adversely impacted.

The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues that may affect our business. There is a degree of uncertainty associated with the legal and regulatory environment around privacy and data protection laws, which continue to develop in ways we cannot predict, including with respect to evolving technologies, such as cloud computing. Privacy and data protection laws may be interpreted and applied inconsistently from country to country and impose inconsistent or conflicting requirements. As a result, our practices may not comply in the future with all such privacy and data protection laws. Varying jurisdictional requirements could increase the costs and complexity of compliance or require us to change our business practices in a manner adverse to our business. A determination that we have violated any privacy or data protection laws could result in significant damage awards, fines and other penalties that could, individually or in the aggregate, materially harm our business and reputation. For example, administrative fines of up to the greater of €20 million or 4% of our global turnover may be imposed for breaches of the GDPR. We may also be liable should any individual who has suffered financial or non-financial damage arising from our infringement of applicable data protection laws exercise his or her right to receive compensation against us.

In addition, our marketing activities and the marketing activities of any third parties on which we rely are subject to various regulations, including privacy and data protection laws, consumer protection laws and competition laws. Such laws may impair our ability, or the ability of third parties on which we rely, to collect information. Such regulations may have a negative effect on businesses and may increase the potential civil liability and cost of operating our business.

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

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

We may also anticipate needs for growth that do not materialize. For example, we expanded our commercial organization in anticipation of a potential U.S. commercial launch of OCA for liver fibrosis due to NASH. However, in June 2020, we received a CRL from the FDA with respect to our NDA for OCA for liver fibrosis due to NASH. Although we re-submitted our NDA seeking accelerated approval of OCA for the treatment of pre-cirrhotic liver fibrosis due to NASH to the FDA in December 2022, there is no assurance that we will be successful or that OCA will be approved for pre-cirrhotic liver fibrosis due to NASH on an accelerated basis, or at all. In August 2020, we adopted the 2020 Workforce Plan to reduce our workforce in light of the receipt of the CRL from the FDA. The 2020 Workforce Plan sought to streamline our operations and reduce operating expenses, while maintaining the critical resources needed to continue to support the NASH and PBC clinical programs, pursue the approval of OCA for the treatment of liver fibrosis due to NASH and support our successful PBC business. The 2020 Workforce Plan resulted in a workforce reduction of approximately 25%, or approximately 170 employees. The 2020 Workforce Plan was implemented during the third quarter of 2020, immediately after its announcement, and was completed in the beginning of 2021. We can provide no assurance that we will correctly forecast the needs for growth given our reliance on approvals from regulatory authorities for our product candidates.

In addition, in order to continue to meet our obligations as a public company and to support any longer-term growth, we may need to maintain and possibly increase our general and administrative capabilities. Our management, personnel and systems may not be adequate to support this future growth.

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

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

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

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

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

We have 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 the members of our executive team, as well as other key employees and consultants. If we lose one or more of our executive officers or other key employees or consultants, our ability to implement our business strategy successfully could be seriously harmed. Any of our executive officers or other key employees or consultants may terminate their employment at any time and replacing such individuals may be difficult and time-consuming because of the limited number of individuals in our industry with the necessary breadth of skills and experience. Competition to hire and retain employees and consultants from this limited pool is intense, and we may be unable to hire, train, retain or motivate such individuals.

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

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

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with the regulations of the FDA, the SEC or other domestic or foreign regulators, provide accurate information to the FDA, the SEC or other domestic or foreign regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive regulation in the United States and abroad intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. Such laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and

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

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

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

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

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

Risks Related to Our Intellectual Property

Ocaliva's market exclusivity period will depend on the validity and enforceability of issued and pending patents covering Ocaliva.

We depend on patents and other intellectual property rights to prevent others from improperly benefiting from our commercial product, Ocaliva, and products or inventions that we develop or acquire. For details about our intellectual property portfolio protecting Ocaliva, see "Item 1. Business—Intellectual Property."

There can be no assurance that any patent previously issued or any patent application will protect Ocaliva from generic competition. Furthermore, there can be no assurance that Ocaliva will not be held to infringe valid patents held by others. If our owned and in-licensed intellectual property do not protect Ocaliva from generic competition, Ocaliva net product sales may decline, and/or we may incur additional costs for patent protection, including patent infringement litigation costs arising out of ANDA submissions by generic companies to manufacture and sell generic products or arising out of 505(b)(2) submissions, which could have a material adverse effect on our business, results of operations and financial condition. If Ocaliva is held to infringe valid patents held by others, we could be subject to liability, and our business may suffer.

The Company received paragraph IV certification notice letters from seven generic drug manufacturers indicating that each such manufacturer submitted to the FDA an ANDA seeking approval to manufacture and sell a generic version of the Company's 5 mg and 10 mg dosage strengths of Ocaliva (obeticholic acid) for PBC prior to the expiration of certain patents listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book") for Ocaliva (the "Ocaliva Patents").

The seven generic drug manufacturers and when we received their initial paragraph IV certification notices are as follows: (1) Apotex Inc. (July 2020), (2) Lupin Limited (July 2020), (3) Amneal Pharmaceuticals of New York, LLC, as U.S. agent for Amneal EU Limited (collectively, "Amneal") (July 2020), (4) Optimus Pharma Pvt Ltd ("Optimus") (July 2020), (5) MSN Pharmaceuticals Inc. and MSN Laboratories Private Limited (July 2020), (6) Dr. Reddy's Laboratories, Inc., and Dr. Reddy's Laboratories, Ltd. (collectively, "Dr. Reddy's") (December 2020) and (7) Zenara Pharma Private Limited ("Zenara") (August 2022).

Each paragraph IV certification notice alleged that the challenged Ocaliva Patents were invalid, unenforceable, and/or would not be infringed by the commercial manufacture, use, or sale of the generic products described in the generic manufacturer's respective ANDA. In each case, within 45 days of receipt of the paragraph IV certification notice, the Company initiated a patent infringement suit against the generic manufacturer in the United States District Court for the District of Delaware seeking injunctions to prevent each generic drug manufacturer from selling a generic version of Ocaliva prior to the expiration of the Ocaliva Patents.

The Company subsequently reached settlement agreements with six of the generic manufacturers. The Company intends to vigorously defend its intellectual property rights protecting Ocaliva against the remaining generic manufacturer. We note, however, that such patent litigations are costly and time-consuming, and successful challenges to the Company's patent or other intellectual property rights could result in the Company losing those rights in the relevant jurisdiction, and could allow third parties to use the Company's proprietary technologies without a license from the Company or its collaborators. The Company can offer no assurances regarding when patent lawsuits such as the remaining Zenara lawsuit will be decided, which side will prevail or whether a generic equivalent of Ocaliva could be approved and enter the market before the expiration of the Ocaliva Patents without license from the Company. If any of the generic manufacturers is successful in the introduction of the generic product described in its respective ANDA, then Ocaliva net product sales may decline, which could have a material adverse effect on our business, results of operations and financial condition.

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

Our commercial success will depend in part on our ability to obtain and maintain patent, trademark and trade secret protection covering Ocaliva, OCA for liver fibrosis due to NASH, if approved, and our other product candidates, as well as our ability to successfully defend our intellectual property against third-party challenges. Our ability to stop third parties from making, using, selling, offering to sell or importing our products is dependent upon the extent to which we have regulatory exclusivity or intellectual property-based exclusivity rights under valid and enforceable patents or other intellectual property that cover our products. If we fail to obtain and maintain adequate intellectual property protection, we may not be able to prevent third parties from launching generic versions of our products, from using our proprietary technologies or from marketing products that are very similar or identical to ours. For example, we have received paragraph IV certification notice letters from seven generic drug manufacturers indicating that each such company has submitted to the FDA an ANDA seeking approval to manufacture and sell a generic version of our 5 mg and 10 mg dosage strengths of Ocaliva (obeticholic acid) for PBC prior to the expiration of certain patents protecting Ocaliva. We timely initiated patent infringement suits against each of these generic drug manufacturers in the United States District Court for the District of Delaware seeking injunctions to prevent each generic drug manufacturer from selling a generic version of Ocaliva prior to the expiration of the Ocaliva Patents. The Company has settled with six of the seven generic drug manufacturers involved. We intend to vigorously defend and enforce our intellectual property rights protecting Ocaliva against the remaining generic manufacturer. However, such patent litigations are costly and time-consuming, and we can offer no assurance as to when the remaining lawsuit will be decided, or whether the lawsuit will be successful. If a generic equivalent of Ocaliva is approved and enters the market before the expiration of our patents protecting Ocaliva, without license from the Company, our business may be materially and adversely affected. See Note 16 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for more information.

The patent positions of pharmaceutical companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States or in foreign jurisdictions, and the legal standards relating to the patentability, validity and enforceability of pharmaceutical patents are evolving. Changes in either the patent laws or in interpretations of patent laws in U.S. and foreign jurisdictions may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be enforced in the patents that we currently own or that may issue from the applications we have filed or may file in the future or those that we may license from third parties. Additionally, our currently pending or future patent applications may not result in issued patents, and any term extensions or reissues that we seek may not be granted. Further, if any patents we obtain or license are deemed invalid or unenforceable, it could impact our ability to commercialize or license our technology or we may not be able to prevent third parties from launching generic versions of our products, or from developing or marketing products that are similar or identical to ours.

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

Others have filed, and in the future, are likely to file, patent applications covering products and technologies that are similar or competitive to ours, or may be important to our business. We cannot be certain that any patent application owned by a third party will not have priority over patent applications filed or in-licensed by us, or that we or our licensors will

not be involved in infringement, interference, derivation, opposition, nullity, invalidity or other similar proceedings before U.S. or non-U.S. patent offices or courts.

The degree to which our patents protect our products may be limited due to a number of factors. For example:

- others may be able to develop and market products that are similar to our products or product candidates but not covered by the claims of our patents;
- we might not have been the first to conceive of the inventions covered by our patents or pending patent applications;
- we might not have been the first to file patent applications for these inventions;
- patents that we obtain may not provide us with competitive advantages or exclusivity in a particular product area or indication or for the length of time we have anticipated; or
- the patents of others may have an adverse effect on our business.

We are the owner of record of numerous issued patents and patent applications with claims directed to pharmaceutical compounds, pharmaceutical compositions, formulations, methods of making these compounds and methods of using these compounds in various indications.

Our issued patents for OCA are expected to expire between 2027 and 2036 if the appropriate maintenance, renewal, annuity, or other government fees are paid. Without patent protection, including patent protection covering the composition of matter, methods of using and formulations of our products and product candidates, our ability to stop others from making, using, selling, offering to sell or importing our products and product candidates may be limited.

Due to the patent laws of a specific country in which we are seeking patent protection, the decisions of a patent examiner in a specific country in which we are seeking patent protection or our own filing strategies, we ultimately may not obtain patent coverage for all of our products and product candidates for which we have filed a patent application. While we regularly pursue patent protection to obtain claim coverage for our inventions, we cannot be certain that such patent rights will be granted or that the scope of any patent granted will prevent third parties from making, using, selling, offering for sale or importing the same or similar products.

If we do not obtain protection under the Hatch-Waxman Act in the United States (or similar legislation outside of the United States) extending the terms of our patents and/or providing data or other exclusivity for our products and product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our products, U.S. patents may be eligible for a limited extension of patent term under the Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Act"). The Hatch-Waxman Act permits an extension of patent term for one patent of up to five years as compensation for patent term lost during product development and the FDA regulatory review process, so long as the total period of patent term extension does not exceed 14 years from the date of approval. However, an extension may not be granted because of, for example, failure to apply within applicable deadlines, failure to apply prior to expiration of relevant patents or failure to satisfy applicable requirements. Moreover, the applicable time period or scope of patent protection afforded could be less than what is requested. If we are unable to obtain patent term extension or the term of any such extension is less than what we request, the period during which we will have the right to exclusively market our products may be shorter than anticipated, 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 was to expire in 2022. In light of the U.S. marketing approval of Ocaliva for PBC in May 2016, and pursuant to the Hatch-Waxman Act, we applied for an extension of the patent term for

this patent in the United States into 2027, which extension has been granted. The issued patents for OCA are expected to expire between 2027 and 2036 if the appropriate maintenance, renewal, annuity, or other government fees are paid.

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

If we choose to file patent infringement lawsuits or engage in other adversarial proceedings to stop another party from making, using, selling, offering for sale or importing the inventions claimed in any of our patents, that individual or company alleged to be infringing has the right to ask the court or adjudicating body to rule that such patents are invalid, not infringed or should not be enforced against that third party. These lawsuits and proceedings are expensive, consume time and resources and divert the attention of management and scientific personnel even if we are successful in defending our rights. In addition, there is a risk that such court or adjudicating body will decide that such patents are invalid, unenforceable or not infringed, and that we do not have the right to stop the other party from making, using, selling, offering for sale or importing the inventions. For example, we have received paragraph IV certification notice letters from seven generic drug manufacturers indicating that each such company has submitted to the FDA an ANDA seeking approval to manufacture and sell a generic version of our 5 mg and 10 mg dosage strengths of Ocaliva (obeticholic acid) for PBC prior to the expiration of certain patents protecting Ocaliva. We timely initiated patent infringement suits against each of these generic drug manufacturers in the United States District Court for the District of Delaware seeking injunctions to prevent each generic drug manufacturer from selling a generic version of Ocaliva prior to the expiration of the Ocaliva Patents. The Company has settled with six of the seven generic drug manufacturers involved. We intend to vigorously defend and enforce our intellectual property rights protecting Ocaliva against the remaining generic manufacturer. However, such lawsuits may be expensive and divert our management's time and attention. In addition, to the extent such lawsuits are not successful, and a generic equivalent of Ocaliva is approved and enters the market before the expiration of our patents protecting Ocaliva, without license from the Company, our business may be materially and adversely affected. See Note 16 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for more information.

Over the past 20 years, the U.S. Supreme Court and the U.S. Congress have modified certain examination procedures utilized by the USPTO in granting patents, which has raised the standard of patentability for some types of inventions. Such modifications may reduce the likelihood that we will be able to obtain patent protection and increase the likelihood of challenges to our patents or the patents we license.

We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and/or delay, halt or increase the costs of our commercialization efforts.

Our success will depend in part on our ability to operate without infringing the proprietary rights of third parties. We cannot guarantee that the use, manufacture, sale, offer for sale or importation of our products will not infringe third-party patents. Furthermore, a third party may claim that we or our manufacturing or commercialization partners are using inventions covered by the third party's patent rights and may go to court to stop us from engaging in our normal operations and activities, including making or selling our products and product candidates. The defense of these lawsuits is often costly and could affect our results of operations and divert the attention of our management and scientific personnel. There is also a risk that a court could decide that we or our manufacturing or commercialization partners are infringing the third party's patents and order us or our partners to stop the activities covered by the patents. In that event, we or our partners may be required to halt or delay commercialization or development of the relevant product or product candidate. In addition, there is a risk that a court could order us or our partners to pay the other party damages for having violated the other party's patents, and we may be subject to indemnification obligations with respect to any such payments made by our partners. There is a vast array of patents and patent applications that claim various pharmaceutical inventions and because the scope of a patent's claims is subject to interpretation by the courts, it is not always clear to industry participants which patents cover various types of products, product candidates or methods of use. In addition, interpretation of a patent's claims can vary from court to court.

If we are sued for patent infringement, we would need to demonstrate that the relevant patent is not enforceable or that our products, product candidates or methods either do not infringe the patent claims of the relevant patent or that the

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

We cannot be certain that others have not filed patent applications for technology covered by our pending applications, or that we were the first to invent or file with respect to a technology, because:

- some patent applications in the United States may be unpublished or otherwise maintained in secrecy until the patents are issued;
- patent applications in the United States are typically not published until 18 months after the priority date; and
- publications in the scientific literature often lag behind actual discoveries.

Our competitors may have filed, and may in the future file, patent applications covering technology similar to ours. Any such patent application may have priority over our patent applications, which could further require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to ours, we may have to participate in an interference, derivation or other similar proceeding declared by the USPTO to determine priority of invention in the United States. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful, resulting in a loss of our U.S. patent position with respect to such inventions. Other countries have similar laws that permit secrecy of patent applications, and such patent applications may be entitled to priority over our applications in such jurisdictions.

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

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

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

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

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

We may rely on trade secrets to protect our proprietary technologies, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect, and may not prevent others from independently and lawfully developing similar or identical products that circumvent our intellectual property. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of proprietary information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information.

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

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

We have numerous trademark and service mark registrations and pending trademark and service mark applications.

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

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

Risks Related to Our Indebtedness

Certain of our debt is secured and imposes covenants.

In August 2021, we retired significant portions of our existing convertible notes by issuing $500.0 million in new 2026 Convertible Secured Notes. These new notes are secured by a first priority security interest in substantially all assets

of Intercept Pharmaceuticals, Inc., including intellectual property. If subsidiaries of Intercept Pharmaceuticals, Inc. meet certain threshold requirements, they may also become guarantors of the notes and subject to a requirement to pledge their security interests.

The new notes also include additional covenants and other requirements compared with our other convertible notes, including limits on incurrence of further indebtedness, limits on payment of dividends, limits on repayment of principal of other indebtedness (other than repayment of the 2023 Convertible Notes at maturity, or before maturity at less than par), limits on transfer of material intellectual property to subsidiaries unless the subsidiaries become guarantors, and requirements to deliver collateral to the collateral agent and enter into deposit account control agreements as regards certain of our bank accounts.

If we fail to comply with these requirements, fail to repay the debt, or otherwise default under these new notes, and the indenture trustee and/or noteholders exercise remedies, they may foreclose on substantially all of our assets, and any such default could also result in a default under our other outstanding indebtedness. Any of which would significantly impair our business and the value of our stock.

We may need significant additional capital to retire or refinance our debt.

In August and September 2022, we repurchased approximately 78% of our 2026 Convertible Secured Notes. We now have outstanding $109.8 million of 2023 Convertible Notes due July 1, 2023; $111.1 million 2026 Convertible Secured Notes due February 15, 2026; and $115.4 million 2026 Convertible Notes due May 15, 2026.

In the future, we may need to raise significant additional capital to repay our outstanding notes maturing in 2026, either from operations, sale of assets, new debt, or new equity. We are not currently profitable, and sales of significant assets could affect our business and future profitability. Given our level of indebtedness, new debt or new equity financing to refinance or pay off our 2026 maturities may not be available on attractive terms, or at all, and, even if available, the issuance of new equity or new convertible notes could dilute existing stockholders.

Our 2026 Convertible Secured Notes are secured by a first priority lien on substantially all assets, so we do not have substantial unsecured assets to pledge to prospective lenders. The 2026 Convertible Secured Notes impair our ability to incur debt maturing prior to their maturity. Lenders may be unwilling to lend on an unsecured basis beyond the maturity of the 2026 Convertible Secured Notes. If we do retire or refinance the 2023 Convertible Notes and the 2026 Convertible Secured Notes, we may still be limited in our ability to retire or refinance the 2026 Convertible Notes.

In addition, adverse capital market conditions may significantly affect our access to capital and ability to retire or refinance our debt. Global capital markets have recently experienced significant volatility, and obtaining capital may become more difficult in the future due to such volatility or other market conditions, including rising interest rates, lower stock prices, increased risk sensitivity among investors, or other factors. Thus, we may not be able to access capital markets when needed, or on favorable terms.

Based on our Company's degree of financial leverage, failure to retire or refinance our debt could impair our ability to invest in our business or engage in strategic transactions. Additionally, inability to repay our debts when due could trigger collection efforts, noteholder remedies, and litigation, and significantly impair the value of our stock.

The issuance of shares of our common stock upon conversion of the convertible notes would dilute the ownership interests of our stockholders and could depress the trading price of our common stock.

We may settle conversions of our outstanding convertible notes in cash, shares of our common stock or a combination of cash and shares of our common stock. The issuance of shares of our common stock upon conversion of the convertible notes would dilute the ownership interests of our stockholders, which could depress the trading price of our common stock. In addition, the market’s expectation that conversions may occur could depress the trading price of our common stock even in the absence of actual conversions. Moreover, the expectation of conversions could encourage the short selling of our common stock, which could place further downward pressure on the trading price of our common stock.

Risks Related to Ownership of Our Common Stock

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

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

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

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

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

We have previously been subject to securities class action lawsuits.

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

In September 2017, a lawsuit and, in January 2018, a follow-on lawsuit, were filed alleging that we and certain of our officers made material misrepresentations and/or omissions of material fact regarding Ocaliva dosing, use and pharmacovigilance-related matters, as well as our operations, financial performance and prospects. These cases were ultimately dismissed and discontinued, respectively.

Additionally, in November 2020, a lawsuit and, in December 2020 and February 2021, follow-on lawsuits, were filed alleging that we and certain of our officers made material misrepresentations and/or omissions of material fact during the period from September 28, 2019 to October 7, 2020 relating to our NDA for OCA for the treatment of liver fibrosis due to NASH and the use of Ocaliva in patients with PBC, as well as our operations, financial performance and prospects. These cases were ultimately dismissed.

We may be subject to additional suits or proceedings brought in the future and, as has been the case with many companies in our industry, we may from time to time receive inquiries and subpoenas and other types of information requests from government authorities and others. While the ultimate outcome of any such investigations, inquiries, information requests and legal proceedings is difficult to predict, adverse resolutions or settlements of those matters may result in, among other things, modification of our business practices, product recalls, significant costs, payments, damages

or fines or other administrative, civil or criminal remedies, liabilities or penalties, which may have a material adverse effect on our business, results of operations and financial condition. In addition, monitoring and defending against legal actions, whether or not meritorious, and responding to investigations, inquiries and information requests is expensive, time-consuming for our management and detracts from our ability to fully focus our internal resources on our business activities, and we cannot predict how long it may take to resolve such matters. Although we may receive insurance coverage for certain adversarial proceedings, coverage could be denied or prove to be insufficient. It is possible that we could, in the future, incur a judgment or enter into settlement of claims for monetary damages. A decision adverse to our interests could result in the payment of substantial damages and could have a material adverse effect on our business, results of operations and financial condition.

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

The market price of our common stock has been, and is likely to continue to be, highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. Since our initial public offering in October 2012, the price of our common stock on the Nasdaq Global Select Market has ranged from $10.81 per share to $497.00 per share. In addition to the other factors discussed in this "Risk Factors" section and elsewhere in this Annual Report on Form 10-K, the factors that may result in wide fluctuations in the price of our common stock include any:

- delay, failure or receipt of regulatory approval for our product candidates, including OCA for liver fibrosis due to NASH;
- delay, failure or receipt of additional marketing authorizations for Ocaliva or our product candidates, including OCA for liver fibrosis due to NASH, in our target markets;
- failure to successfully commercialize our approved products in the United States, the European Union and our other target markets, or our inability to maintain regulatory approval for Ocaliva or our other approved products in such markets;
- clinical trial failure, including any such failure resulting from issues, delays or difficulties in identifying patients, enrolling patients, treating patients, retaining patients, meeting specific endpoints in the jurisdictions in which we intend to seek approval or completing and timely reporting the results of our clinical trials, such as our NASH and PBC trials;
- the effects of COVID-19 and related public health safety measures and business closures and disruptions;
- inability to obtain additional funding;
- delay in filing an investigational new drug application, 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 any such submission;
- potential side effects associated with Ocaliva for PBC, OCA for liver fibrosis due to NASH or our other product candidates;
- inability to obtain adequate product supply of Ocaliva, OCA for liver fibrosis due to NASH or any of our other product candidates or the inability to do so at acceptable prices;
- results of clinical trials of our competitors' products and product candidates;
- regulatory or advisory committee actions or recommendations with respect to our products or product candidates, including Ocaliva or OCA for liver fibrosis due to NASH, or our competitors' products or product candidates;
- changes in laws or regulations applicable to our products or product candidates;

- failure to meet or exceed financial projections or guidance we may provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;
- actual or anticipated fluctuations in our financial condition and operating results;
- actual or anticipated changes in our growth rate relative to our competitors;
- actual or anticipated fluctuations in our competitors' operating results or changes in their growth rate;
- competition from existing products or new products that may emerge;
- announcements by us, our collaborators or our competitors of significant acquisitions, strategic collaborations, joint ventures, collaborations or capital commitments;
- issuance of new or updated research or reports by securities analysts;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- additions or departures of key management or scientific personnel;
- disputes or other developments related to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- announcement or expectation of additional financing efforts;
- disputes, governmental inquiries or investigations, legal proceedings or litigation, including any securities, intellectual property, employment, product liability or other litigation;
- sales of our common stock by us, our insiders or our other stockholders;
- failure to adopt appropriate information security systems, including any systems that may be required to prevent or defend against system failures or security or security or data breaches due to cyber-attacks, or cyber intrusions, including ransomware, phishing attacks and other malicious intrusions;
- failure to comply with data protection laws;
- market conditions for biopharmaceutical stocks in general; and
- general economic, industry, market and political conditions.

Any of these factors could also affect the trading price of the Convertible Notes.

Furthermore, stock markets in general and the market for biotechnology companies in particular have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of securities of many companies. These fluctuations often have been unrelated or disproportionate to the operating performance of those companies. A number of factors, including global health catastrophes (e.g., COVID-19), general economic, political and market conditions, recessions, interest rate changes or international currency fluctuations may negatively impact the market price of our securities, 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. In the past, we have been subject to this type of litigation, which could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business. As a result of this volatility, you could incur substantial losses.

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

We may in the future raise funds through the issuance and sale of additional shares of our common stock or other securities convertible into or exchangeable for our common stock. For example, in August 2021, we issued $500.0 million aggregate principal amount of the 2026 Convertible Secured Notes, in May 2019, we issued and sold an aggregate of 2,879,760 shares of common stock and $230.0 million aggregate principal amount of the 2026 Convertible Notes, in April 2018, we issued and sold an aggregate of 4,257,813 shares of common stock and in July 2016, we issued and sold $460.0 million aggregate principal amount of the 2023 Convertible Notes. Conversions of the Convertible Notes will dilute the ownership interests of existing shareholders to the extent that we elect to deliver shares of our common stock (or a combination of cash and shares of our common stock) in connection therewith. In addition, the existence of the Convertible Notes may encourage short selling by market participants because the conversion of the Convertible Notes could depress the price of our common stock. We may also issue shares of common stock, stock options, restricted stock, restricted stock units or other stock-based awards under our existing or future equity incentive plans or other employee or director compensation plans. The issuance of additional shares of common stock (including pursuant to conversions of the Convertible Notes) or other securities convertible into or exchangeable for our common stock, or the perception that such issuances may occur, may materially and adversely affect the price of our common stock and the Convertible Notes.

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

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

- authorizing the issuance of "blank check" convertible preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders, to the extent that no stockholder, together with its affiliates, holds more than 50% of our voting stock;
- eliminating the ability of stockholders to call a special meeting of stockholders;
- permitting our board of directors to accelerate the vesting of outstanding equity awards upon certain transactions that result in a change of control; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

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

Certain provisions of the Convertible Notes could also make it more difficult or more expensive for a third party to acquire us. For example, if an acquisition event constitutes a "fundamental change" under the terms of the Convertible Notes, holders of the Convertible Notes will have the right to require us to purchase their Convertible Notes for cash. Similarly, if an acquisition event constitutes a "make-whole fundamental change" under the terms of the Convertible

Notes, we may be required to increase the conversion rate for holders who convert their Convertible Notes in connection with such make-whole fundamental change.

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

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

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

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

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

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

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

We have significant net operating loss carryforwards ("NOLs") for U.S. Federal, state and foreign income tax purposes. The enactment of the Tax Cuts and Jobs Act enacted in 2017 (the "TCJA") modified the ability of companies to utilize U.S. Federal NOLs arising in tax years beginning on or after January 1, 2018, by providing that such NOLs may be carried-forward indefinitely and used to offset up to 80 percent of taxable income in any given future year. Existing NOLs that arose in tax years beginning prior to January 1, 2018, were not affected by the TCJA and are generally eligible to be carried-forward for up to 20 years and used to fully offset taxable income in future years. If not utilized, our pre-2018 NOLs will expire for U.S. Federal income tax purposes between 2030 and 2037. In addition, the Biden administration is proposing changes to the Internal Revenue Code. It is not yet clear what effect such tax legislation would have on our NOLs, financial condition, and results of operations. We also have certain U.S. state and foreign NOLs in varying amounts depending on the different state and foreign tax laws.

In addition, our ability to utilize our NOLs may be limited under Section 382 of the Internal Revenue Code or applicable state and foreign tax law. The Section 382 limitations apply if an "ownership change" occurs. Generally, an ownership change occurs when certain shareholders increase their aggregate ownership by more than 50 percentage points

over their lowest ownership percentage in a testing period (typically three years). We have evaluated whether one or more ownership changes under Section 382 have occurred since our inception and have determined that there have been at least two such changes. Although we believe that these ownership changes have not resulted in material limitations on our ability to use these NOLs, our ability to utilize these NOLs may be limited due to future ownership changes or for other reasons. As a result, we may not be able to take full advantage of our NOL carryforwards for U.S. Federal, state, and foreign income tax purposes.

General Risk Factors

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

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

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

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

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

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

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, employment practices liability, property, auto, workers' compensation, cyber liability, products liability and directors' and officers' insurance. We do not know, however, if our current levels of coverage are adequate or if we will be able to obtain insurance with adequate levels of coverage in the future, if at all. Any significant uninsured liability, including significant uninsured liabilities resulting from COVID-19 or related public health safety measures or business closures and disruptions, may require us to pay substantial amounts, which could materially and adversely affect our financial position and results of operations. Furthermore, any increase in the volatility of our stock price, among other factors, may result in us being required to pay substantially higher premiums for our directors' and officers' insurance, and may make it difficult for us to obtain adequate coverage on reasonable terms, if at all.

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

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

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

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

In particular, our compliance with Section 404 of the Sarbanes-Oxley Act has required and will continue to require that we incur substantial accounting-related expenses and expend significant management efforts. Our testing, or the testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls that we would be required to remediate in a timely manner. If we are not able to comply with the requirements of the Sarbanes-Oxley Act, we could be subject to sanctions or investigations by the SEC, the Nasdaq Global Select Market or other regulatory authorities, which would require additional financial and management resources and could adversely affect the market price of our securities. Furthermore, if we cannot provide reliable financial reports or prevent fraud, including as a result of remote working by our employees in connection with COVID-19 and related public health safety measures, our business and results of operations would likely be materially and adversely affected.

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.

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, such as the TCJA and its required capitalization and amortization of research and development costs that went into effect for taxable years beginning after December 31, 2021, the accounting for stock options and other stock-based compensation, changes in accounting standards, future levels of research and development spending, changes in the mix and level of pre-tax earnings in different jurisdictions, the outcome of audits or other examinations by the U.S. Internal Revenue Service and tax regulators in other jurisdictions, the accuracy of our estimates for unrecognized tax benefits, the realization of deferred tax assets and changes to our ownership or capital structure. The Biden administration is proposing changes to the Internal Revenue Code that could include material increases to corporate tax rates. It is not yet clear what effect such tax legislation would have on our financial condition and results of operations.

The impact on our effective income tax rate resulting from these factors may be significant and could adversely affect our results of operations.

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

The market for our common stock and the Convertible Notes 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 and the price of the Convertible Notes may decline. If one or more of the analysts covering us fail to regularly publish reports on us, demand for our common stock and the Convertible Notes may decline, which could cause our stock price and the price of the Convertible Notes and trading volume to decline.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our corporate headquarters are located at 305 Madison Avenue in Morristown, New Jersey, where we lease and occupy an aggregate of approximately 26,000 square feet of office space. The lease covering this property is scheduled to expire in July 2027. We have one renewal option for an additional five-year term, to be based on market rates prevailing at such time.

We lease additional office space in San Diego, California and London, United Kingdom.

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

Item 3. Legal Proceedings

For a description of our significant legal proceedings, see Note 16 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K and incorporated by reference herein.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

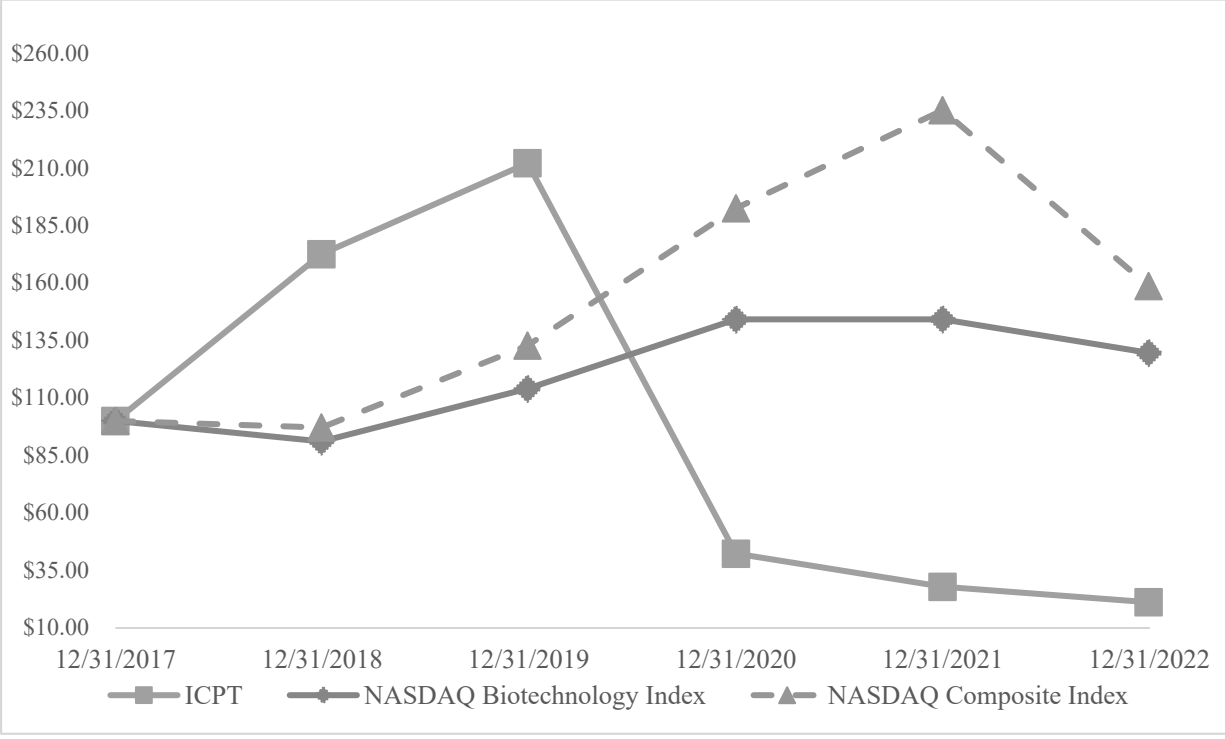
Market Information and Stockholders

Our common stock trades on the Nasdaq Global Select Market under the symbol "ICPT". As of December 31, 2022, there were 41,523,337 shares of our common stock issued and outstanding and approximately 72 stockholders of record. A significantly larger number of stockholders may hold their shares in "street name" through banks, brokers and other nominees. The number of stockholders of record does not include stockholders who hold their shares in "street name."

Stock Price Performance Graph

The following graph compares the cumulative total stockholder return for our common stock to the cumulative total stockholder return for the Nasdaq Composite Index and the Nasdaq Biotechnology Index, in each case, for the period from December 31, 2017 through December 31, 2022. The graph assumes an initial investment of $100 in our common stock at the closing price of $58.42 on December 31, 2017 and in the Nasdaq Composite Index and the Nasdaq Biotechnology Index on December 31, 2017 and the reinvestment of dividends. The stock performance shown below is not intended to forecast or be indicative of the possible future performance of our common stock, and we do not make or endorse any predications as to future stockholder returns. The following stock performance information shall not be deemed to be "soliciting material," "filed" with the U.S. Securities and Exchange Commission (the "SEC"), incorporated by reference into any filing under the Securities Act of 1933, as amended (the "Securities Act"), or the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or subject to the liabilities of Section 18 of the Exchange Act, except to the extent that we specifically incorporate it by reference into a document filed under the Securities Act or the Exchange Act.

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



	December 31,					
	2017	2018	2019	2020	2021	2022
$100 investment in stock or index						
Intercept Pharmaceuticals, Inc..	$ 100.00	$ 172.53	$ 212.12	$ 42.28	$ 27.88	$ 21.17
Nasdaq Composite Index	$ 100.00	$ 97.16	$ 132.81	$ 192.47	$ 235.15	$ 158.65
Nasdaq Biotechnology Index	$ 100.00	$ 91.14	$ 114.02	$ 144.15	$ 144.18	$ 129.59

Dividend Policy

We have never declared or paid any cash dividends on our common stock, and we do not anticipate paying any cash dividends in the foreseeable future. The first supplemental indenture for the recently issued 2026 Convertible Secured Notes restricts the Company from declaring or paying cash dividends.

Recent Sales of Unregistered Securities

On August 17, 2021, the Company sold $500.0 million of 2026 Convertible Secured Notes in exchange for old convertible notes and in a new subscription for cash, as described below in “Current and Long-Term Debt” in the notes to our financial statements. These new notes were issued in a private placement to institutional investors in reliance on the exemption from registration provided by Section 4(a)(2) of the Securities Act.

As of August 20, 2021, the Company agreed with its financial advisor in the exchange and issuance, J. Wood Capital Advisors LLC, to settle its financial advisory fee for services rendered through issuance of 769,823 shares of common stock, equivalent to $10.0 million. These shares were issued in a private placement in reliance on the exemption from registration provided by Section 4(a)(2) of the Securities Act.

Of the new 2026 Convertible Secured Notes, $117.6 million were issued at par for cash. Substantially all proceeds were used either for the repurchase of 4,521,502 shares of common stock in connection with the notes issuance for $75.8 million, or the repurchase in September 2021 of additional 2023 Convertible Notes for $38.1 million.

The 2026 Convertible Secured Notes are convertible into shares of common stock, with the terms of conversion described under “Current and Long-Term Debt”, which have not been registered under the Securities Act. The 2026 Convertible Secured Notes contain various covenants, including limitations upon the payment of dividends.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the three months ended December 31, 2022.

Item 6. [Reserved]

Not applicable.

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

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

Overview

We are a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat progressive non-viral liver diseases with high unmet medical need utilizing our proprietary bile acid chemistry. Our first marketed product, Ocaliva® (obeticholic acid or "OCA"), is a farnesoid X receptor ("FXR") agonist approved in the United States, the United Kingdom, the European Union and several other jurisdictions for the treatment of primary biliary cholangitis ("PBC") in combination with ursodeoxycholic acid ("UDCA") in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA.

In addition to commercializing OCA for PBC under the Ocaliva brand name, we are also currently developing OCA for additional indications, including nonalcoholic steatohepatitis ("NASH"). We are also developing product candidates in various stages of clinical and preclinical development. We believe that OCA and our other product candidates have the potential to treat orphan and other more prevalent liver diseases such as NASH for which there are currently limited therapeutic options.

Ocaliva was approved for PBC by the U.S. Food and Drug Administration ("FDA") in May 2016 under the accelerated approval pathway. We commenced sales and marketing of Ocaliva in the United States shortly after receiving approval, and Ocaliva is now available to U.S. patients primarily through a network of specialty pharmacy distributors. Ocaliva received conditional approval for PBC from the European Commission in December 2016. Since January 2017, Ocaliva has also received regulatory approval in several markets outside the United States and Europe, including (but not limited to) Canada, Israel and Australia. Ocaliva received orphan drug designation in both the United States and the European Union for the treatment of PBC. In addition, we continue to work to execute on our post-marketing regulatory commitments with respect to Ocaliva.

In June 2022, we announced topline results from our COBALT trial and HEROES-US study. In September 2022, we had a supplemental NDA ("sNDA") pre-submission meeting with the FDA in which we reviewed our post-marketing requirements with respect to Ocaliva. We intend to submit the data from COBALT and HEROES-US studies as well as additional data, including data from other real world evidence studies, as part of a broader evidence package in the sNDA in support of full approval of Ocaliva for the treatment of PBC, which we anticipate submitting to the FDA in 2023. If this data package does not support fulfillment of our post-marketing obligations, we may not be able to maintain our previously granted marketing approvals of Ocaliva for PBC.

Our lead development product candidate is OCA for the potential treatment of NASH. In February 2019, we announced topline results from the planned 18-month interim analysis of our pivotal Phase 3 clinical trial of OCA in patients with liver fibrosis due to NASH, known as the REGENERATE trial (the "Original Analysis"). The REGENERATE trial is ongoing and is expected to continue through clinical outcomes for verification and description of the clinical benefit of OCA. In June 2020, we received a complete response letter ("CRL") from the FDA stating that our NDA for OCA for the treatment of liver fibrosis due to NASH could not be approved in its present form. We had our end of review meeting with the FDA in October 2020 to discuss the FDA's risk-benefit assessment in the CRL based on its review of the available data, as well as our proposed resubmission of our NDA for the treatment of liver fibrosis due to NASH. The meeting was constructive and the FDA provided us with helpful guidance regarding supplemental data we could provide to further characterize OCA's efficacy and safety profile that could support resubmission based on our Phase 3 REGENERATE 18-month biopsy data, together with a safety assessment from our ongoing studies.

Following our end of review meeting, we have held a productive dialogue with FDA regarding the REGENERATE study to clarify data, a new consensus read methodology for liver biopsies, and analyses required to re-submit our NDA.

In connection with the resubmission of our NDA, we conducted a new interim analysis of our ongoing pivotal Phase 3 REGENERATE trial of OCA using a biopsy consensus read methodology in the same intent-to-treat ("ITT") population as the Original Analysis (the "New Interim Analysis").

In July 2022, we announced topline results from the New Interim Analysis. In this new interim analysis of the ITT population from REGENERATE, 22.4% of subjects randomized to once-daily oral OCA 25 mg met the primary endpoint of achieving at least one stage of fibrosis improvement with no worsening of NASH at month 18 on liver biopsy compared with 9.6% of subjects on placebo ($p<0.0001$). The results were consistent with the Original Analysis, which also showed that OCA 25 mg had a statistically significant effect on fibrosis improvement ($p=0.0002$). Based on the results of the New Interim Analysis, in December 2022 we re-submitted our NDA for OCA in pre-cirrhotic liver fibrosis due to NASH.

In July 2022, we had a pre-submission meeting with the FDA in which we reviewed the planned structure and the timing of the submission of our NDA and had an ongoing dialogue as we prepared to re-submit. The Company will need to overcome the risk-benefit assessment of the FDA from the prior review of the NDA for OCA for the treatment of liver fibrosis due to NASH. Although we believe that the insights we have gained from the re-analysis and from the larger and more robust safety database provide an improved risk-benefit, there can be no assurances that the FDA will change its view on risk-benefit and will approve such NDA on an accelerated basis, or at all.

In September 2022, we announced that REVERSE, a Phase 3 study evaluating the safety and efficacy of OCA in patients with compensated cirrhosis due to NASH, did not meet its primary endpoint of a $\geq$ 1-stage histological improvement in fibrosis with no worsening of NASH following up to 18 months of therapy. No new safety signals for OCA were observed in this population of patients with cirrhosis.

In November 2022, we announced plans to focus development of our next-generation FXR agonist, INT-787, in severe alcohol-associated hepatitis (sAH).

In December 2022, we re-submitted an NDA to the FDA for OCA for the treatment of patients with pre-cirrhotic liver fibrosis due to NASH. The resubmission is supported by a robust body of evidence from the OCA NASH clinical development program, including two positive interim 18-month analyses from the pivotal Phase 3 REGENERATE study in patients with pre-cirrhotic liver fibrosis due to NASH. In both REGENERATE analyses, treatment with OCA 25 mg demonstrated a statistically significant improvement in liver fibrosis by at least one stage without worsening of NASH—an improvement that was more pronounced in individuals with more advanced disease at baseline.

In January 2023, we announced that the FDA accepted our NDA for OCA seeking accelerated approval for the treatment of patients with pre-cirrhotic liver fibrosis due to NASH. The FDA indicated that it considers this a complete, Class 2 resubmission and has assigned a PDUFA target action date of June 22, 2023, for the NDA. The timeline for the review of the NDA by the FDA remains subject to change.

As part of our product development activities, we expect to continue to invest in evaluating the potential of OCA in progressive non-viral liver diseases.

We are evaluating the efficacy, safety and tolerability of OCA in combination with bezafibrate in patients with PBC in a Phase 2 study outside of the United States that has completed enrollment. In the United States, we have an ongoing Phase 1 study to better characterize the exposure response of the fixed-dose combination, which has completed enrollment, and we have an open Investigational New Drug ("IND") application with the FDA. We are also conducting a second Phase 2 study evaluating a fixed-dose combination of OCA and bezafibrate for the treatment of patients with PBC who have not achieved an adequate biochemical response to UDCA. Our longer-term goal is developing and seeking regulatory approval for a fixed dose combination regimen in PBC and potentially in other diseases.

In addition, we have other compounds in early stages of research and development in our pipeline, including our INT-787 compound, an FXR agonist. We submitted an IND for INT-787 in the first half of 2022, which is now active, and we announced plans to focus development of INT-787 in severe alcohol-associated hepatitis (sAH). We initiated a Phase 2a trial evaluating the safety, tolerability, efficacy and pharmacokinetics of INT-787 in subjects with sAH.

Sale of our ex-U.S. commercial operations to Advanz Pharma

The sale of our ex-U.S. commercial operations to Advanz Pharma and affiliates (collectively, "Advanz") and sublicense of the right to commercialize Ocaliva for PBC and, if approved, OCA for NASH, outside of the United States for $405 million (subject to adjustments including for cash, working capital, and assumed liabilities) plus a potential $45 million earnout allowed us to capitalize on an opportunity that supports multiple pathways for the future and strengthened our balance sheet in 2022 and going forward. The terms of this transaction will allow us to focus our resources on the United States, our largest market, while retaining upside from the potential NASH opportunity ex-U.S., via royalties on any future net sales of OCA, should Advanz obtain marketing authorizations for this indication in ex-U.S. regions.

The ex-U.S. commercial business operations met the criteria within Accounting Standards Codification 205-20 to be reported as discontinued operations because the transaction represented a strategic shift in business that would have a major effect on our operations and financial results. Therefore, we have reported the historical results of the ex-U.S. commercial business including the results of operations and cash flows as discontinued operations, and related assets and liabilities were retrospectively reclassified as assets and liabilities of discontinued operations for all prior periods presented herein. Applicable amounts in prior periods have been recast to conform to this discontinued operations presentation. Refer to Note 3 of our consolidated financial statements included in this Annual Report on Form 10-K for additional information.

Recent Developments

In January and February 2023, we entered into settlement agreements with five additional generic manufacturers resolving our patent litigations with them over their ANDAs seeking approval to market generic versions of Ocaliva prior to expiration of our patents.

Financial Overview

Revenue

We commenced our commercial launch of Ocaliva for the treatment of PBC in the United States in June 2016. In December 2016, the European Commission granted conditional approval for Ocaliva for the treatment of PBC. Since January 2017, Ocaliva has also received regulatory approval in several markets outside the United States and Europe, including (but not limited to) Canada, Israel, and Australia. We sell Ocaliva to a limited number of specialty pharmacies which dispense the product directly to patients. The specialty pharmacies are referred to as our customers.

Product Revenue, Net

We recognize revenue upon delivery of Ocaliva to our customers, net of discounts, rebates and incentives associated with the product. We provide the right of return to our customers for unopened product for a limited time before and after its expiration date.

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

We recognized net sales of Ocaliva of $285.7 million, $260.8 million and $234.0 million for the years ended December 31, 2022, 2021 and 2020, respectively.

Selling, General and Administrative Expenses

We have incurred and expect to continue to incur significant selling, general and administrative expenses as a result of, among other initiatives, the commercialization of Ocaliva for PBC in the United States. In addition, we have incurred significant selling, general and administrative expenses and may in the future incur incremental expenses in connection with the preparation for the potential commercialization of OCA for liver fibrosis due to NASH, if approved, and our other future approved products, if any, and any maintenance of our general and administrative infrastructure.

Research and Development Expenses

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

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

Results of Operations

Certain amounts in prior periods have been reclassified to reflect the impact of the discontinued operations treatment in order to conform to the current period presentation.

Comparison of the Years Ended December 31, 2022 and 2021

The following table summarizes our results of operations for the years ended December 31, 2022 and 2021:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Revenue:		
Product revenue, net	$ 285,710	$ 260,750
Total revenue	285,710	260,750
Operating expenses:		
Cost of sales	984	1,205
Selling, general and administrative	176,303	177,488
Research and development	176,639	182,747
Restructuring	—	(284)
Total operating expenses	353,926	361,156
Other (expense) income:		
Interest expense	(21,385)	(54,419)
(Loss) gain on extinguishment of debt	(91,778)	16,511
Other income, net	6,521	1,962
Total other (expense), net	(106,642)	(35,946)
Loss from continuing operations	$ (174,858)	$ (136,352)
Income from discontinued operations, net of tax	$ 396,674	$ 44,926
Net income (loss)	$ 221,816	$ (91,426)

Revenues

Product revenue, net was $285.7 million and $260.8 million for the years ended December 31, 2022 and 2021, respectively. For the years ended December 31, 2022 and 2021, product revenue, net was solely comprised of U.S. Ocaliva net sales. The increase in product revenues was driven by operational growth, primarily due to higher pricing and increased unit sales volumes, partially offset by higher gross to net deductions.

Cost of sales

Cost of sales was $1.0 million and $1.2 million for the years ended December 31, 2022 and 2021, respectively. Our cost of sales for the years ended December 31, 2022 and 2021 consisted primarily of packaging, labeling, materials and related expenses.

Selling, general and administrative expenses

Selling, general and administrative expenses were $176.3 million and $177.5 million for the years ended December 31, 2022 and 2021, respectively. The $1.2 million net decrease between periods was primarily driven by lower headcount, partially offset by higher costs for litigation and commercial activities.

Research and development expenses

Research and development expenses were $176.6 million and $182.7 million for the years ended December 31, 2022 and 2021, respectively. The $6.1 million net decrease between periods was primarily driven by lower NASH and cholestasis development costs as well as R&D cost-sharing reimbursements of $5.4 million from Advanz, which was offset by a $7.2 million reduction in recognition of UK R&D tax credits under the U.K. Small and Medium-sized Enterprise R&D Tax Credit scheme, or the SME scheme, and the U.K. Research and Development Expenditure Scheme, or the RDEC scheme, and higher costs for INT-787 activities.

Interest expense

Interest expense was $21.4 million and $54.4 million for the years ended December 31, 2022 and 2021, respectively. For the year ended December 31, 2022, interest expense related to the principal amounts outstanding for the 2023 Convertible Notes, 2026 Convertible Notes and 2026 Convertible Secured Notes and no longer includes any accretion of debt discounts associated with conversion features, which was $30.8 million for the year ended December 31, 2021, after the adoption of ASU No. 2020-06, "Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity ("ASU 2020-06"). For the year ended December 31, 2021, interest expense related to the principal amounts outstanding for the 2023 Convertible Notes, 2026 Convertible Notes and 2026 Convertible Secured Notes.

(Loss) gain on extinguishment of debt

(Loss) gain on extinguishment of debt was ($91.8) million and $16.5 million for the years ended December 31, 2022 and 2021, respectively. For the year ended December 31, 2022, the net loss on extinguishment of debt mainly relates to the repurchases of the 2026 Convertible Secured Notes. For the year ended December 31, 2021, the gain on extinguishment of debt relates to the exchange of debt and repurchase of 2023 Convertible Notes.

Other income, net

Other income, net was $6.5 million and $2.0 million for the years ended December 31, 2022 and 2021, respectively. Such income is primarily attributable to interest income earned on cash, cash equivalents and investment debt securities along with additional income of $3.0 million recognized during the year ended December 31, 2022 for transitional services provided by us to Advanz.

Income from discontinued operations, net of tax

Income from discontinued operations, net of tax was $396.7 million and $44.9 million for the years ended December 31, 2022 and 2021, respectively. The increase in income from discontinued operations was primarily a result of the $369.3 million gain (inclusive of income tax expense of $8.0 million) recognized on the sale of our ex-U.S. commercial operations and sublicense to Advanz.

Income taxes

For the years ended December 31, 2022 and 2021, no income tax expense or benefit was recognized for our continuing operations. Our deferred tax assets are comprised primarily of net operating loss carryforwards. We maintain a full valuation allowance on our deferred tax assets since we have not yet achieved sustained profitable operations. As a result, we have not recorded any income tax benefit since our inception.

Comparison of the Years Ended December 31, 2021 and 2020

The following table summarizes our results of operations for the years ended December 31, 2021 and 2020:

	Years Ended December 31,	
	2021	2020
	(in thousands)	
Revenue:		
Product revenue, net	$ 260,750	$ 233,970
Total revenue	260,750	233,970
Operating expenses:		
Cost of sales	1,205	2,353
Selling, general and administrative	177,488	260,502
Research and development	182,747	189,029
Restructuring	(284)	11,813
Total operating expenses	361,156	463,697
Other (expense) income:		
Interest expense	(54,419)	(48,054)
Gain on extinguishment of debt	16,511	—
Other income, net	1,962	4,381
Total other (expense) income, net	(35,946)	(43,673)
Loss from continuing operations	$ (136,352)	$ (273,400)
Income (loss) from discontinued operations, net of tax	$ 44,926	$ (1,480)
Net loss	$ (91,426)	$ (274,880)

Revenues

Product revenue, net was $260.8 million and $234.0 million for the years ended December 31, 2021 and 2020, respectively. For the years ended December 31, 2021 and 2020, product revenue, net was solely comprised of U.S. Ocaliva net sales. The increase in product revenues was driven by operational growth, primarily due to higher unit sales volumes and higher net pricing.

Cost of sales

Cost of sales was $1.2 million and $2.4 million for the years ended December 31, 2021 and 2020, respectively. Our cost of sales for the years ended December 31, 2021 and 2020 consisted primarily of packaging, labeling, materials and related expenses.

Selling, general and administrative expenses

Selling, general and administrative expenses were $177.5 million and $260.5 million for the years ended December 31, 2021 and 2020, respectively. The $83.0 million net decrease between periods was primarily driven by decreases in expenses relating to our activities associated with the potential approval and commercialization of OCA for liver fibrosis due to NASH.

Research and development expenses

Research and development expenses were $182.7 million and $189.0 million for the years ended December 31, 2021 and 2020, respectively. The $6.3 million net decrease between periods was primarily driven by lower personnel costs, including stock compensation expense and lower costs for NASH related R&D activities, partially offset by the recognition of lower R&D tax credits and higher costs for cholestasis related R&D activities.

Interest expense

Interest expense was $54.4 million and $48.1 million for the years ended December 31, 2021 and 2020, respectively. For the year ended December 31, 2021, interest expense related to the principal amounts outstanding for the 2023 Convertible Notes, 2026 Convertible Notes and 2026 Convertible Secured Notes. For the year ended December 31, 2020, interest expense related to the principal amounts outstanding for the 2023 Convertible Notes and 2026 Convertible Notes.

Gain on extinguishment of debt

Gain on extinguishment of debt was $16.5 million and $0 for the years ended December 31, 2021 and 2020, respectively. For the year ended December 31, 2021, the gain on extinguishment of debt relates to the exchange of debt and repurchase of 2023 Convertible Notes.

Other income, net

Other income, net was $2.0 million and $4.4 million for the years ended December 31, 2021 and 2020, respectively. Such income is primarily attributable to interest income earned on cash, cash equivalents and investment debt securities.

Income from discontinued operations

Income (loss) from discontinued operations was $44.9 million and $(1.5) million for the years ended December 31, 2021 and 2020, respectively. The increase in income was primarily a result of the increase in product revenues of $24.0 million and a decrease of $22.2 million of operating expenses associated with the ex-U.S. commercial business.

Income taxes

For the years ended December 31, 2021 and 2020, no income tax expense or benefit was recognized for our continuing operations. Our deferred tax assets are comprised primarily of net operating loss carryforwards. We maintain a full valuation allowance on our deferred tax assets since we have not yet achieved sustained profitable operations. As a result, we have not recorded any income tax benefit since our inception.

Liquidity and Capital Resources

Sources of liquidity

Since inception, we have incurred significant operating losses. Our continuing operations have never been profitable and we do not expect them to be profitable in the foreseeable future. To date, we have financed our operations primarily through public and private securities offerings, sales of product and payments received under our licensing and collaboration agreements and the sale of our ex-U.S. commercial operations.

Continued cash generation is highly dependent on the success of our commercial product, Ocaliva, as well as the success of our product candidates if approved. The absence of cash flows from discontinued operations are not expected to affect future liquidity and capital resources.

We have devoted substantially all of our resources to the development of our product candidates, including the conduct of our clinical trials, the commercialization of Ocaliva for PBC, preparation for a potential launch of OCA for liver fibrosis due to NASH and general and administrative operations, including the protection of our intellectual property. We intend to continue to develop OCA and our other existing product candidates, alone or in combination, for non-viral liver diseases. If OCA or any of our other product candidates fails in clinical trials or does not gain or maintain regulatory approval, or if OCA or any of our other product candidates does not achieve market acceptance, we may never become profitable. Our net losses and negative operating cash flows have had, and will continue to have, an adverse effect on our stockholders' deficit and working capital.

Our executive officers and our Board of Directors periodically review our sources and potential uses of cash in connection with our annual budgeting process. Generally speaking, our principal funding source is cash from operating activities, and our principal cash requirements include operating expenses and interest payments.

We expect to continue to incur losses for the foreseeable future, and we expect these losses to be significant as we, among other things, develop and seek regulatory approval for our product candidates, including OCA for liver fibrosis due to NASH, maintain our regulatory approval and commercialize our approved products. We believe our prospects and ability to significantly grow revenues will be dependent on our ability to successfully develop and commercialize OCA for indications other than PBC, such as NASH, and to identify strategic business development opportunities to leverage our capabilities in rare diseases. As a result, we expect a significant amount of resources to continue to be devoted to our development programs for OCA and to developing our pipeline.

Cash Flows

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

	Years Ended December 31,		
	2022	2021	2020
		(in thousands)	
Net cash from continuing operations (used in) provided by:			
Operating activities	$ (33,743)	$ (98,986)	$ (198,207)
Investing activities	(101,384)	70,726	162,817
Financing activities	(267,316)	1,118	(693)
Effect of exchange rate changes	(6,302)	(2,023)	614
Net increase in cash, cash equivalents and restricted cash classified as discontinued operations	370,196	57,920	26,343
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (38,549)	$ 28,755	$ (9,126)

Operating Activities. Net cash used in operating activities of $33.7 million for continuing operations during the year ended December 31, 2022 was primarily a result of our $174.9 million net loss from continuing operations, partially offset by a loss of $91.8 million on the extinguishments of debt, a net increase in operating assets and liabilities of $21.9 million, $21.9 million in stock-based compensation, $2.6 million of amortization for deferred financing costs, $2.4 million of write-

offs of fixed assets and $1.7 million for non-cash operating lease costs. Cash flows for the year ended December 31, 2022 include net cash receipts of $3.8 million reflecting payments from His Majesty's Revenue and Customs (the "HMRC") for the U.K. R&D tax credit claims.

Net cash used in operating activities of $99.0 million for continuing operations during the year ended December 31, 2021 was primarily a result of our $136.4 million net loss from continuing operations and a net decrease in operating assets and liabilities of $19.7 million, partially offset by $28.0 million in stock-based compensation, $13.0 million for accretion of the discount on the 2023 Convertible Notes, $8.4 million for accretion of the discount on the 2026 Convertible Notes, $9.4 million for accretion on the 2026 Convertible Secured Notes, $4.7 million for non-cash operating lease costs and $2.8 million of depreciation. Cash flows for the year ended December 31, 2021 include cash receipts of $4.0 million reflecting payments from the HMRC for the U.K. R&D tax credit claims.

Net cash used in operating activities of $198.2 million for continuing operations during the year ended December 31, 2020 was primarily a result of our $273.4 million net loss from continuing operations and a net decrease in operating assets and liabilities of $14.8 million, partially offset by $49.2 million in stock-based compensation, $16.6 million for accretion of the discount on the 2023 Convertible Notes, $9.4 million for accretion of the discount on the 2026 Convertible Notes, $5.3 million for non-cash operating lease costs, $4.0 million for amortization of premium on investment debt securities, $2.9 million of depreciation and $2.5 million for amortization of deferred financing costs. Cash flows for the year ended December 31, 2020 include cash receipts of $20.7 million reflecting payments from the HMRC for the U.K. R&D tax credit claims.

Investing Activities. For the year ended December 31, 2022, net cash used in investing activities for continuing operations primarily reflects the purchases of investment debt securities of $552.7 million partially offset by the sales and maturities of investment debt securities of $451.9 million.

For the year ended December 31, 2021, net cash provided by investing activities for continuing operations primarily reflects the sales and maturities of investment debt securities of $420.6 million, partially offset by the purchases of investment debt securities of $349.5 million.

For the year ended December 31, 2020, net cash provided by investing activities for continuing operations primarily reflects the sales and maturities of investment debt securities of $497.4 million, partially offset by the purchases of investment debt securities of $330.7 million.

Financing Activities. Net cash used in financing activities for continuing operations of approximately $267.3 million in the year ended December 31, 2022, primarily consisted of payments of $264.5 million for the repurchase of 2026 Convertible Secured Notes and $3.9 million for the repurchase of 2023 Convertible Notes.

Net cash provided by financing activities for continuing operations in the year ended December 31, 2021 consisted primarily of $116.7 million of proceeds, net of issuance costs, from the sale of 2026 Convertible Secured Notes, partially offset by payments of $75.8 million for the repurchase of common stock and $38.1 million for the repurchase of 2023 Convertible Notes.

Net cash used in financing activities for continuing operations in the year ended December 31, 2020 consisted primarily of $2.0 million from payments of employee withholding taxes related to stock-based awards, partially offset by $1.3 million of net proceeds from the exercise of options to purchase common stock.

Net change in cash, cash equivalents and restricted cash – discontinued operations. Net increase in cash, cash equivalents and restricted cash for discontinued operations in the year ended December 31, 2022 consisted of approximately $363.2 million of cash provided by investing activites for proceeds received from the sale of the ex-U.S. business to Advanz and $7.0 million of cash provided by operating activities, primarily a result of $396.7 million net income from discontinued operations and $4.5 million in stock-based compensation, partially offset by a net decrease in operating assets and liabilities of $28.3 million given the net liabilities sold.

Net increase in cash, cash equivalents and restricted cash for discontinued operations in the year ended December 31, 2021 consisted of net cash provided by operating activities of approximately $57.9 million, primarily a result of $44.9 million net income from discontinued operations, $5.9 million in stock-based compensation and a net increase in operating assets and liabilities of $5.8 million.

Net increase in cash, cash equivalents and restricted cash for discontinued operations in the year ended December 31, 2020 consisted of net cash provided by operating activities of approximately $26.3 million, primarily a result of a net increase in operating assets and liabilities of $14.9 million and $11.7 million in stock-based compensation, partially offset by a net loss from discontinued operations of $1.5 million.

2022 Debt Retirement

In June 2022, the Company entered into an agreement with a certain holder of 2023 Convertible Notes to repurchase $3.8 million principal for $3.8 million in cash, which purchase closed on June 3, 2022.

In August and September 2022, we entered into a series of exchange agreements and agreed with a limited number of existing noteholders of our 2026 Convertible Secured Notes to exchange approximately $388.9 million aggregate principal amount of existing notes for $258.2 million in cash and 11,329,399 shares of newly issued common stock (equivalent to $219.4 million), for total consideration of $477.6 million. Net of these exchanges, the principal balance of the 2026 Convertible Secured Notes was reduced by $388.9 million from $500.0 million to $111.1 million. The result of these activities was to lower principal debt outstanding by 54% or $388.9 million to $336.3 million and decrease annual cash interest expense by 58% or $13.6 million to $9.8 million on an annual basis. In addition, these activities reduced overall potential shareholder dilution associated with the 2026 Convertible Secured Notes.

Future Funding Requirements

We are currently developing OCA for additional indications, including NASH, and other product candidates through various stages of clinical and preclinical development. Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. In addition, we have incurred and anticipate that we will continue to incur significant research and development, product sales, marketing, manufacturing and distribution expenses relating to the commercialization of Ocaliva for PBC. As part of our longer-term strategy, we anticipate that we will incur significant expenses in connection with our research and development efforts, the commercialization of our other products such as OCA for liver fibrosis due to NASH, if approved, and the maintenance of our general and administrative infrastructure. We may also engage in business development activities that involve potential in- or out-licensing of products or technologies or acquisitions of other products, technologies or businesses.

As of December 31, 2022, we had $490.9 million in cash, cash equivalents, restricted cash and investment debt securities. We expect to continue to incur significant operating expenses in the fiscal year ending December 31, 2023. These expenses are planned to support, among other initiatives, the continued commercialization of Ocaliva for PBC, our continued clinical development of OCA for PBC and NASH and our other earlier stage research and development programs. Although we believe that our existing capital resources, together with our net sales of Ocaliva for PBC, will be sufficient to fund our anticipated operating requirements for the next twelve months following the filing of this report, and repay the remaining balance of the 2023 Convertible Notes, we may need to raise additional capital to fund our operating requirements beyond that period. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. As of December 31, 2022, our funds are primarily held in U.S. treasuries, U.S. government agency bonds, corporate bonds, commercial paper and money market accounts.

We recently used a combination of cash proceeds received from the sale of our international business as well as common stock to fund the repurchases of the 2026 Convertible Secured Notes. Our short-term obligations include $109.8 million of 2023 Convertible Notes outstanding scheduled to mature on July 1, 2023, and $226.5 million of convertible notes scheduled to mature in 2026, all of which will need to be paid off or refinanced, if not converted. Furthermore, in light of our receipt of the CRL from the FDA in June 2020 with respect to our NDA for OCA for liver fibrosis due to NASH and the numerous risks and uncertainties associated with pharmaceutical product development and commercialization, any delays in, or unanticipated costs associated with, our development, regulatory or

commercialization efforts could significantly increase the amount of capital required by us to fund our operating requirements. Accordingly, we may seek to access the public or private capital markets whenever conditions are favorable, to issue new securities, or to refinance or repurchase existing securities, even if we do not have an immediate need for additional capital at that time.

Our forecasts regarding the period of time that our existing capital resources will be sufficient to meet our operating requirements and the timing of our future funding requirements, both near and long-term, will depend on a variety of factors, many of which are outside of our control. Such factors include, but are not limited to, those factors listed above under "Cautionary Note Regarding Forward-Looking Statements".

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

Future Contractual Obligations

Our estimated future obligations as of December 31, 2022 include both current and long term obligations. For our debt as noted in Note 9—Current and Long-Term Debt, we have short-term obligations for interest and principal payments of $117.8 million and long-term obligations of $240.2 million for interest and principal payments.

We enter into contracts in the normal course of business with contract research organizations for our clinical trials. We may incur expenses related to clinical studies of our product candidates. The timing and amounts of these disbursements are contingent upon the achievement of certain milestones, patient enrollment and services rendered or as expenses are incurred by the CROs or clinical trial sites. Therefore, we cannot estimate the potential timing and amount of these payments.

We source the manufacture and commercial supply of API from manufacturers, for use in Ocaliva and, if approved, OCA for liver fibrosis due to NASH. Our contracts either do not require us to purchase a specific percentage of our annual commercial requirements of API, are made on a purchase order basis or may require future purchase obligations in the event of the achievement of agreed regulatory and product development milestones. We cannot, at this time, determine when or if the related milestones will be achieved or whether the events triggering the commencement of payment obligations will occur.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our audited consolidated financial statements, which we have prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of our audited consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses. We have identified certain estimates as critical to our business operations and the understanding of our past or present results of operations related to (i) revenue recognition, (ii) stock-based compensation, (iii) issuance of convertible debt and (iv) income taxes. These estimates are considered critical because they had a material impact, or they have the potential to have a material impact, on our consolidated financial statements and because they require us to make significant judgments, assumptions or estimates. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances based on information available at the time they were made. We evaluate these estimates and judgments on an ongoing basis. However, our actual results could differ from these estimates, and these differences may be material.

Revenue Recognition

Product Revenue, Net

Under ASC 606, we have written contracts with each of our customers that have a single performance obligation — to deliver products upon receipt of a customer order — and this obligation is satisfied when delivery occurs and the

customer receives Ocaliva. We evaluate the creditworthiness of each of our customers to determine whether collection is reasonably assured. The wholesale acquisition cost that we charge our customers for Ocaliva is adjusted to arrive at our estimated net product revenues by deducting (i) estimated government rebates and discounts, (ii) estimated costs of incentives offered to certain indirect customers including patients, and (iii) trade allowances, such as invoice discounts for prompt payment and customer fees. The amount of variable consideration included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period.

Rebates and Discounts

We contract with the Centers for Medicare & Medicaid Services and other government agencies to make Ocaliva available to eligible patients and offer associated rebates and discounts on Ocaliva to those agencies. As a result, we estimate any rebates and discounts and deduct these estimated amounts from our gross product revenues at the time the revenues are recognized. Our estimates of rebates and discounts are based on the government mandated discounts, which are statutorily-defined and applicable to these government funded programs, and our historical experience with actual payments and redemptions. Estimates associated with government programs have a higher risk of being subject to adjustment because of the time delay between recording the accrual and the final settlement. These reserves reflect our best estimates of the amount of consideration to which the relevant third party is entitled to based on the terms of the applicable contract. These estimates are recorded in accounts payable, accrued expenses and other liabilities on our consolidated balance sheets. To date, actual government rebates have not differed materially from our estimates. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our estimates, we adjust these estimates, which would affect net product revenues and earnings in the period such variances become known.

Other Incentives

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

Trade Allowances

We provide invoice discounts on Ocaliva sales to certain of our customers for prompt payment and record these discounts as a reduction to gross product revenues. These discounts are based on contractual terms. We anticipate that our customers will earn these discounts and fees and, therefore, we deduct the full amount of these discounts and fees from total gross product revenues. Reserves for prompt payment discounts are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and accounts receivable.

Returns

The Company provides the right of return to its customers for unopened product for a limited time before and after its expiration date. Returns are estimated based on historical experience and product shelf lives. In arriving at our estimate, the assessment considered the product type, life-cycle, price, distribution channel, channel inventory and the customer returns policy along with benchmarking against industry data. To date, actual returns have not differed materially from our estimates.

Valuation of Stock-Based Compensation

We account for stock-based compensation in accordance with ASC Topic 718, *Compensation — Stock Compensation*. We estimate the fair value of stock option awards using the Black-Scholes option pricing model on the date of the grant.

Valuation models, like the Black-Scholes-Merton model, require the use of subjective assumptions that could materially impact the estimation of fair value and related compensation expense to be recognized. The Black-Scholes option pricing model requires the use of assumptions, including with respect to price volatility of the underlying stock, assumed dividend yield, expected term of the options and the risk-free interest rate, as described below:

- The expected volatility is estimated based on actual daily historical volatility information of our own ordinary shares equal to the expected term of our options.

- The assumed dividend yield is based on not issuing any dividends and not expecting to issue any dividends over the life of the options. As a result, we have estimated the dividend yield to be zero.

- The expected term of options granted represents the period of time the options are expected to be outstanding and is based on the simplified method, whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the option (generally 10 years).

- The risk-free interest rate is based on the yield curve for U.S. Treasury securities at the date of grant with maturity dates approximately equal to the expected term of the award at the grant date.

There have been no material changes in our estimates or assumptions since the prior reporting period. We do not believe there is a reasonable likelihood there will be a material change in the future estimates or assumptions.

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

Convertible Debt

Prior to adoption of ASU 2020-06, the Convertible Notes were accounted for in accordance with ASC Subtopic 470-20, *Debt with Conversion and Other Options*. Prior to the effective date of the changes in ASU 2020-06 (January 1, 2022), ASC Subtopic 470-20 required the issuer of convertible debt that may be settled in shares or cash upon conversion at the issuer's option, such as the Convertible Notes, to account for the liability (debt) and equity (conversion option) components separately. The value assigned to the debt component was the estimated fair value, as of the issuance date, of a similar debt instrument without the conversion option. The amount of the equity component (and resulting debt discount) was calculated by deducting the fair value of the liability component from the principal amount of the convertible debt instrument. The resulting debt discount is amortized as additional non-cash interest expense over the expected life of the notes utilizing the effective interest method.

The carrying amount of the liability component was calculated by measuring the fair value of a similar liability that does not have an associated convertible feature using the income approach. The allocation was performed in a manner that reflected our non-convertible borrowing rate for similar debt. For the income-based approach, we use a convertible bond lattice model that includes assumptions such as volatility and the risk-free rate. The equity component is not remeasured as long as it continues to meet the conditions for equity classification.

For additional information, see Note 9 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Income Taxes

We utilize the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial statement carrying amounts and tax bases of assets and liabilities using enacted tax rates in effect for years in which the temporary differences are expected to reverse.

We determine the need for a valuation allowance by assessing the probability of realizing deferred tax assets, taking into consideration all available positive and negative evidence, including historical operating results, expectations of future

taxable income, carryforward periods available, various income tax strategies and other relevant factors. Judgment is required in making this assessment and to the extent future expectations change, we would have to assess the recoverability of our deferred assets at that time. At December 31, 2022 and 2021, we maintained a full valuation allowance on our deferred tax assets.

Our tax returns are subject to examination by U.S. Federal, state, and foreign taxing jurisdictions. The impact of an uncertain tax position taken or expected to be taken on an income tax return must be recognized in our financial statements at the largest amount that is more likely than not to be sustained. An uncertain income tax position will not be recognized in our financial statements unless it is more likely than not to be sustained. We consider the facts, circumstances, and information available at the reporting date. The level of evidence that is necessary and appropriate to support an entity's assessment of the technical merits of a tax position is a matter of judgment that depends on all available information. As a result, whether a tax position will ultimately be sustained may be uncertain. At December 31, 2022 and 2021, we had no reserves for unrecognized tax benefits.

Recent Accounting Pronouncements

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

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. We currently do not hedge interest rate exposure because of the short-term maturities of our cash equivalents and investment debt securities. Our investment debt securities are subject to interest rate risk and will fall in value if market interest rates increase. At any time, sharp changes in interest rates can affect the fair value of the investment portfolio and its interest earnings. We do not believe that an increase in market rates would have any significant impact on the realized value of our investment debt securities. If a hypothetical increase in interest rates of 100 basis points were to have occurred on December 31, 2022, this change would not have had a material effect on the fair value of our investment portfolio as of that date due to the conservative and short-term nature of these investments.

We do not believe that our cash, cash equivalents and investment debt securities have significant risk of default or illiquidity. We maintain an investment portfolio in accordance with our investment policy. The primary objectives of our investment policy are to preserve principal and maintain proper liquidity to meet operating needs. Although our investments are subject to credit risk, our investment policy specifies credit quality standards for our investments, maturity restrictions and limits the amount of credit exposure from any single issue or issuer. While we believe our cash, cash equivalents and investment debt securities do not contain excessive risk, we cannot provide absolute assurance that, in the future, our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash and cash equivalents at one or more financial institutions that are in excess of federally insured limits.

As a result of our limited remaining ex-U.S. operations, we may contract with CROs, investigational sites, suppliers, facilities and other vendors and suppliers in Europe and internationally. We are therefore subject to fluctuations in foreign currency exchange rates in connection with these agreements. We do not hedge our foreign currency exchange rate risk.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We reviewed inflation impacts, and made a reasonable determination that these are or will be immaterial. We do not believe that inflation has had a material effect on our results of operations during 2022, 2021 or 2020.

Item 8. Financial Statements and Supplementary Data

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

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

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our Chief Executive Officer and Chief Financial Officer evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2022. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2022, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control Over Financial Reporting

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

All internal controls, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to consolidated financial statement preparation and presentation. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, assessed the effectiveness of our internal control over financial reporting as of December 31, 2022, based on criteria established in the Internal Control — Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on that assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2021.

Attestation Report of Independent Registered Public Accounting Firm

The effectiveness of our internal control over financial reporting as of December 31, 2022 has been audited by KPMG LLP, an independent registered public accounting firm, as stated in their report included elsewhere in this Annual Report on Form 10-K.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the quarter ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

Not applicable.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

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

The remainder of the information required by this item is incorporated by reference to our definitive proxy statement related to our 2023 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

Item 11. Executive Compensation

The information required by this item is incorporated by reference to our definitive proxy statement related to our 2023 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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

The information required by this item is incorporated by reference to our definitive proxy statement related to our 2023 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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

The information required by this item is incorporated by reference to our definitive proxy statement related to our 2023 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

Item 14. Principal Accountant Fees and Services

The information required by this item is incorporated by reference to our definitive proxy statement related to our 2023 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) 1. Index to Consolidated Financial Statements

Certain amounts in prior periods have been reclassified to reflect the impact of the discontinued operations treatment in order to conform to the current period presentation.

2. Index to Consolidated Financial Statements

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

3. Exhibits

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

Exhibit Index

Exhibit Number	Exhibit Description	Incorporated herein by reference		
		Form†	Exhibit	Filing Date
3.1	Restated Certificate of Incorporation, as amended	Form 10-Q	3.1	August 10, 2020
3.2	Restated Bylaws	Form 10-Q	3.2	August 10, 2020
4.1	Form of Common Stock Certificate	Form S-8(1)	4.3	November 7, 2012
4.2	Indenture, dated as of July 6, 2016, between the Registrant and U.S. Bank National Association, as trustee	Form 8-K	4.1	July 6, 2016
4.3	First Supplemental Indenture (including the Form of Note), dated as of July 6, 2016, between the Registrant and U.S. Bank National Association, as trustee	Form 8-K	4.2	July 6, 2016
4.4	Form of Senior Indenture	Form S-3(2)	4.1	May 10, 2017
4.5	Form of Subordinated Indenture	Form S-3(2)	4.2	May 10, 2017
4.6	Form of Senior Note	Form S-3(2)	4.3	May 10, 2017
4.7	Form of Subordinated Note	Form S-3(2)	4.4	May 10, 2017
4.8	Second Supplemental Indenture (including the Form of Note), dated as of May 14, 2019, between the Registrant and U.S. Bank National Association, as trustee	Form 8-K	4.2	May 14, 2019
4.9*	Description of Securities of the Registrant			
4.10	Indenture, dated as of August 17, 2021, between the Registrant and U.S. Bank National Association, as trustee	Form 8-K	4.1	August 23, 2021
4.11	First Supplemental Indenture (including the Form of Note), dated as of August 17, 2021, between the Registrant and U.S. Bank National Association, as trustee and as collateral agent	Form 8-K	4.2	August 23, 2021
4.12	Security Agreement, dated as of August 17, 2021, among the Registrant, the Guarantors that may from time to time be a party thereto and U.S. Bank National Association, as collateral agent	Form 8-K	10.1	August 23, 2021
10.1#	Intercept Pharmaceuticals, Inc. Amended and Restated Equity Incentive Plan	Form 10-Q	10.11	August 3, 2022
10.2#	Form of Stock Option Grant Notice and Agreement for Directors	Form 10-Q	10.13	August 3, 2022
10.3#	Form of Stock Option Grant Notice and Agreement for Employees and Consultants	Form 10-Q	10.12	August 3, 2022

10.4#	Form of Restricted Stock Unit Award Grant Notice and Agreement for Directors	Form 10-Q	10.15	August 3, 2022
10.5#	Form of Restricted Stock Unit Award Grant Notice and Agreement for Employees and Consultants	Form 10-Q	10.14	August 3, 2022
10.6#	Form of Performance Stock Unit Grant Notice and Agreement	Form 10-Q	10.16	August 3, 2022
10.7#	2022 Cash Incentive Plan	Form 8-K	10.1	January 31, 2022
10.8#	2022 Cash Incentive Plan - Form of Performance-Based Award Agreement	Form 8-K	10.2	January 31, 2022
10.9#	2023 Cash Incentive Plan	Form 8-K	10.1	February 2, 2023
10.10#	2023 Cash Incentive Plan – Form of Performance-Based Award Agreement	Form 8-K	10.2	February 2, 2023
10.11#	Employment Agreement, effective April 14, 2017, between the Registrant and David Ford	Form 10-Q	10.1	August 3, 2017
10.12#	Amended and Restated Employment Agreement, dated as of December 9, 2020, between the Registrant and Jerome Durso	Form 8-K	10.1	December 10, 2020
10.13#	Employment Agreement, effective as of December 18, 2020, between the Registrant and Jared Freedberg	Form 10-K	10.21	February 25, 2021
10.14#	Employment Agreement, effective February 15, 2021, between the Registrant and Linda Richardson	Form 10-Q	10.3	May 6, 2021
10.15#	Employment Agreement, effective May 17, 2021, between the Registrant and Andrew Saik	Form 10-Q	10.1	July 29, 2021
10.16#	Employment Agreement, effective June 2, 2021, between the Registrant and M. Michelle Berrey	Form 10-Q	10.2	July 29, 2021
10.17#	Employment Agreement, effective April 21, 2022, between the Registrant and Rocco Venezia	Form 10-Q	10.4	May 6, 2022
10.18#	Form of Indemnification Agreement for directors and executive officers of the Registrant	Form S-1(3)	10.7	September 4, 2012
10.19	Base Call Option Confirmation, dated June 30, 2016, between the Registrant and Royal Bank of Canada	Form 8-K	10.1	July 6, 2016
10.20	Base Call Option Confirmation, dated June 30, 2016, between the Registrant and UBS AG, London Branch	Form 8-K	10.3	July 6, 2016
10.21	Base Call Option Confirmation, dated June 30, 2016, between the Registrant and Credit Suisse Capital LLC	Form 8-K	10.5	July 6, 2016

10.22	Additional Call Option Confirmation, dated July 1, 2016, between the Registrant and Royal Bank of Canada	Form 8-K	10.2	July 6, 2016
10.23	Additional Call Option Confirmation, dated July 1, 2016, between the Registrant and UBS AG, London Branch	Form 8-K	10.4	July 6, 2016
10.24	Additional Call Option Confirmation, dated July 1, 2016, between the Registrant and Credit Suisse Capital LLC	Form 8-K	10.6	July 6, 2016
10.25+	Agreement of Lease, dated February 7, 2022, between United States Fire Insurance Company as Landlord and the Registrant as Tenant	Form 8-K	10.1	February 9, 2022
10.26+	Sublicense Agreement, dated May 5, 2022, among Intercept Pharma Europe Limited ("IPEL"), Mercury Pharma Group Limited, and the Registrant	Form 10-Q	10.2	August 3, 2022
10.27+	Agreement for Supply of Manufactured Products, dated May 5, 2022, between IPEL and Amdipharm Limited	Form 10-Q	10.3	August 3, 2022
21.1*	Subsidiaries of the Registrant			
23.1*	Consent of Independent Registered Public Accounting Firm			
24.1*	Power of Attorney (included in signature page to this Annual Report on Form 10-K)			
31.1*	Certification of Principal Executive Officer required by Rule 13a-14(a) or Rule 15d-14(a)			
31.2*	Certification of Principal Financial Officer required by Rule 13a-14(a) or Rule 15d-14(a)			
32.1*(4)	Certifications required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. 1350)			
101*	The following materials from the Registrant's Annual Report on Form 10-K for the year ended December 31, 2022, formatted in Inline XBRL (eXtensible Business Reporting Language): (i) Consolidated Balance Sheets as of December 31, 2022 and 2021, (ii) Consolidated Statements of Operations for the Years Ended December 31, 2022, 2021 and 2020, (iii) Consolidated Statement of Comprehensive Income (Loss) for the Years Ended December 31, 2022, 2021 and 2020, (iv) Consolidated Statements of Changes in Stockholders' Equity (Deficit) for the Years Ended December 31, 2022, 2021 and 2020, (v) Consolidated Statements of Cash Flows for the Years Ended December 31, 2022, 2021 and 2020 and (vi) Notes to Consolidated Financial Statements			

104*	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

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* Filed herewith.

\+ Portions of the exhibit have been omitted pursuant to Regulation S-K, Item 601(b)(10)(iv).

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

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

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

(2) Registration Statement on Form S-3 filed by the Registrant, Registration No. 333-217861.

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

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

Item 16. Form 10-K Summary

None.

SIGNATURES

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

INTERCEPT PHARMACEUTICALS, INC.

Date: March 2, 2023

By:/s/ Jerome Durso
Jerome Durso
President and Chief Executive Officer
(Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Jerome Durso, Andrew Saik and Rocco Venezia, and each of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her, and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and all other documents in connection therewith, with the Securities and Exchange Commission, granting unto each said attorney-in-fact and agent full power and authority to do and perform each and every act and thing required or necessary to be done in and about the premises, as fully and to all intents and purposes as the undersigned could do in person, and hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities indicated on March 2, 2023.

Signature	Title
/s/ Jerome Durso Jerome Durso	President and Chief Executive Officer and Director (Principal Executive Officer)
/s/ Andrew Saik Andrew Saik	Chief Financial Officer (Principal Financial Officer)
/s/ Rocco Venezia Rocco Venezia	Senior Vice President, Chief Accounting Officer and Treasurer (Principal Accounting Officer)
/s/ Paolo Fundarò Paolo Fundarò	Chairman of the Board of Directors
/s/ Srinivas Akkaraju, M.D., Ph.D. Srinivas Akkaraju, M.D., Ph.D.	Director
/s/ Luca Benatti, Ph.D. Luca Benatti, Ph.D.	Director
/s/ Daniel Bradbury Daniel Bradbury	Director
/s/ Keith Gottesdiener, M.D. Keith Gottesdiener, M.D.	Director

/s/ Nancy Miller-Rich Nancy Miller-Rich	Director
/s/ Mark Pruzanski, M.D. Mark Pruzanski, M.D.	Director
/s/ Dagmar Rosa-Bjorkeson Dagmar Rosa-Bjorkeson	Director
/s/ Gino Santini Gino Santini	Director
/s/ Glenn Sblendorio Glenn Sblendorio	Director

INTERCEPT PHARMACEUTICALS, INC.

Index to Consolidated Financial Statements

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

Opinions on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Intercept Pharmaceuticals, Inc. and subsidiaries (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations, comprehensive income (loss), changes in stockholders' equity (deficit), and cash flows for each of the years in the three-year period ended December 31, 2022, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission, and our report dated March 2, 2023 expressed an unqualified opinion on the effectiveness of the Company's internal control over financial reporting.

Basis for Opinion

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

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

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Assessing deductions from revenue related to certain rebates and discounts accruals

As discussed in Note 2 to the consolidated financial statements, the Company records net product revenue by deducting rebates and discounts, among other items. Certain rebates and discounts are related to arrangements with the Centers for Medicare & Medicaid Services and other government agencies, and are estimated and accrued with a corresponding reduction of gross product revenues when revenue is recognized. The Company had $7.5 million in

rebates and discounts accruals as of December 31, 2022 which were recorded in accounts payable, accrued expenses and other liabilities on the consolidated balance sheet.

We identified the assessment of deductions from revenue related to certain rebates and discounts accruals as a critical audit matter because evaluating the Company's assumptions involved especially challenging auditor judgment.

The following are the primary procedures we performed to address this critical audit matter. We evaluated the design and tested the operating effectiveness of certain internal controls over the Company's rebates and discounts accruals process, including controls related to the significant assumptions used in the Company's estimation of certain rebates and discounts. We evaluated the Company's ability to estimate rebates and discounts by comparing the previously recorded accruals to the actual amounts that were settled and ultimately paid by the Company. We assessed the Company's current period estimates by comparing the accrued amounts to historical payments and redemptions. We also performed sensitivity analyses based on potential changes in certain assumptions and assessed the impact relative to the Company's accruals as of December 31, 2022.

/s/ KPMG LLP

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

New York, New York
March 2, 2023

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

Opinion on Internal Control Over Financial Reporting

We have audited Intercept Pharmaceuticals, Inc. and subsidiaries' (the Company) internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2022 and 2021, the related consolidated statements of operations, comprehensive income (loss), changes in stockholders' equity (deficit), and cash flows for each of the years in the three-year period ended December 31, 2022, and the related notes (collectively, the consolidated financial statements), and our report dated March 2, 2023 expressed an unqualified opinion on those consolidated financial statements.

Basis for Opinion

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

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

Definition and Limitations of Internal Control Over Financial Reporting

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

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

/s/ KPMG LLP

New York, New York
March 2, 2023

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Balance Sheets

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 50,517	$ 84,709
Restricted cash	5,343	8,119
Investment debt securities, available-for-sale	435,049	334,980
Accounts receivable, net of allowance for credit losses of $54 and $58, respectively	26,862	28,337
Prepaid expenses and other current assets	22,356	22,778
Current assets of discontinued operations	—	29,095
Total current assets	540,127	508,018
Fixed assets, net	987	3,281
Inventory	6,462	7,883
Security deposits	1,013	4,284
Other assets	5,122	3,557
Total assets	$ 553,711	$ 527,023
Liabilities and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable, accrued expenses and other liabilities	$ 116,977	$ 103,780
Short-term interest payable	3,531	8,601
Current portion of long-term debt	109,569	—
Current liabilities of discontinued operations	—	55,780
Total current liabilities	230,077	168,161
Long-term liabilities:		
Long-term debt	223,104	539,782
Long-term other liabilities	7,453	3,042
Total liabilities	$ 460,634	$ 710,985
Commitments and contingencies (Note 16)		
Stockholders' equity (deficit):		
Common stock par value $0.001 per share; 90,000,000 shares authorized; 41,523,337 and 29,572,953 shares issued and outstanding as of December 31, 2022 and December 31, 2021, respectively	42	30
Additional paid-in capital	2,238,179	2,308,653
Accumulated other comprehensive loss, net	(8,256)	(2,873)
Accumulated deficit	(2,136,888)	(2,489,772)
Total stockholders' equity (deficit)	93,077	(183,962)
Total liabilities and stockholders' equity (deficit)	$ 553,711	$ 527,023

See accompanying notes to consolidated financial statements.

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Statements of Operations

	Years Ended December 31,		
	2022	2021	2020
	(in thousands, except per share data)		
Revenue:			
Product revenue, net	$ 285,710	$ 260,750	$ 233,970
Total revenue	285,710	260,750	233,970
Operating expenses:			
Cost of sales	984	1,205	2,353
Selling, general and administrative	176,303	177,488	260,502
Research and development	176,639	182,747	189,029
Restructuring	—	(284)	11,813
Total operating expenses	353,926	361,156	463,697
Operating loss	(68,216)	(100,406)	(229,727)
Other (expense) income:			
Interest expense	(21,385)	(54,419)	(48,054)
(Loss) gain on extinguishment of debt	(91,778)	16,511	—
Other income, net	6,521	1,962	4,381
Total other (expense) income, net	(106,642)	(35,946)	(43,673)
Loss from continuing operations	$ (174,858)	$ (136,352)	$ (273,400)
Income (loss) from discontinued operations, net of income taxes	$ 396,674	$ 44,926	$ (1,480)
Net income (loss)	$ 221,816	$ (91,426)	$ (274,880)
Net income (loss) per common and potential common share (basic and diluted):			
Net loss from continuing operations	$ (5.17)	$ (4.28)	$ (8.29)
Net income (loss) from discontinued operations	$ 11.72	$ 1.41	$ (0.04)
Net income (loss)	$ 6.56	$ (2.87)	$ (8.34)
Weighted average common and potential common shares outstanding:			
Basic and diluted	33,837	31,894	32,970

See accompanying notes to consolidated financial statements.

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Statements of Comprehensive Income (Loss)

	Years Ended December 31,		
	2022	2021	2020
		(in thousands)	
Net income (loss)	$ 221,816	$ (91,426)	$ (274,880)
Other comprehensive loss:			
Net changes related to available-for-sale investment debt securities:			
Unrealized losses on investment debt securities	(1,360)	(754)	(202)
Reclassification adjustment for realized (gains) losses on investment debt securities included in other income, net	(17)	15	(135)
Net unrealized losses on investment debt securities	$ (1,377)	$ (739)	$ (337)
Foreign currency translation and other			
Release of currency translation adjustments associated with sale of business	(7,319)	—	—
Foreign currency translation gains (losses)	3,313	343	(996)
Other comprehensive loss	(5,383)	(396)	(1,333)
Comprehensive income (loss)	$ 216,433	$ (91,822)	$ (276,213)

See accompanying notes to consolidated financial statements.

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Statements of Changes in Stockholders' Equity (Deficit)
For the Years Ended December 31, 2022, 2021 and 2020 (in thousands)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss, Net	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount				
Balance - December 31, 2019	32,853	$ 33	$ 2,176,133	$ (1,144)	$ (2,123,466)	$ 51,556
Stock-based compensation	—	—	60,850	—	—	60,850
Net proceeds from exercise of stock options	176	—	(1,052)	—	—	(1,052)
Employee withholding taxes related to stock-based awards	(13)	—	(1,994)	—	—	(1,994)
Other comprehensive loss	—	—	—	(1,333)	—	(1,333)
Net loss	—	—	—	—	(274,880)	(274,880)
Balance - December 31, 2020	33,016	$ 33	$ 2,233,937	$ (2,477)	$ (2,398,346)	$ (166,853)
Stock-based compensation	—	—	33,888	—	—	33,888
Issuance of common stock under equity plan	392	—	18	—	—	18
Employee withholding taxes related to stock-based awards	(83)	—	(1,737)	—	—	(1,737)
Repurchase of common stock	(4,522)	(4)	(75,821)	—	—	(75,825)
Extinguishment of allocated costs related to exchange of convertible notes	—	—	(37,213)	—	—	(37,213)
Extinguishment of allocated costs related to repurchase of convertible notes	—	—	(1,933)	—	—	(1,933)
Bifurcation of conversion option upon issuance of convertible notes, net of issuance costs	—	—	147,458	—	—	147,458
Issuance of common stock for services related to exchange of convertible notes	770	1	9,999	—	—	10,000
Proceeds from capped call transactions	—	—	57	—	—	57
Other comprehensive loss	—	—	—	(396)	—	(396)
Net loss	—	—	—	—	(91,426)	(91,426)
Balance - December 31, 2021	29,573	$ 30	$ 2,308,653	$ (2,873)	$ (2,489,772)	$ (183,962)
Reclassification of the equity components of the Convertible Notes to liability upon adoption of ASU 2020-06	—	—	(307,371)	—	131,068	(176,303)
Stock-based compensation	—	—	26,390	—	—	26,390
Issuance of common stock under equity plan	546	1	—	—	—	1
Employee withholding taxes related to stock-based awards	(38)	—	(557)	—	—	(557)
Net proceeds from exercise of stock options	112	—	1,684	—	—	1,684
Issuance of common stock for repurchase of convertible notes	11,330	11	209,380	—	—	209,391
Other comprehensive loss	—	—	—	(5,383)	—	(5,383)
Net income	—	—	—	—	221,816	221,816
Balance - December 31, 2022	41,523	$ 42	$ 2,238,179	$ (8,256)	$ (2,136,888)	$ 93,077

See accompanying notes to consolidated financial statements.

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Statements of Cash Flows

	Years Ended December 31,		
	2022	2021	2020
Cash flows from operating activities:			
Net income (loss)	$ 221,816	$ (91,426)	$ (274,880)
Less: Income (loss) from operations of discontinued operations, net of tax	396,674	44,926	(1,480)
Adjustments to reconcile net income (loss) to net cash used in operating activities:			
Stock-based compensation	21,889	28,032	49,186
(Accretion) amortization of (discount) premium on investment debt securities	(630)	4,674	4,006
Amortization of deferred financing costs	2,606	2,544	2,540
Write-off of fixed assets	2,400	—	—
Depreciation	592	2,814	2,943
Non-cash operating lease cost	1,667	4,711	5,270
Accretion of debt discount	—	30,787	25,964
Loss (gain) on early extinguishment of debt	91,778	(16,511)	—
Gain on lease termination	(1,100)	—	—
Provision for allowance on credit losses, net of write-offs	(4)	4	54
Changes in operating assets:			
Accounts receivable	1,479	(3,417)	(1,791)
Prepaid expenses and other current assets	44	229	(3,141)
Inventory	602	378	205
Security deposits	3,270	391	(255)
Other assets	21	—	1,393
Changes in operating liabilities:			
Accounts payable, accrued expenses and other current liabilities	23,288	(13,785)	(4,951)
Operating lease liabilities	(1,717)	(6,171)	(6,230)
Interest payable	(5,070)	2,686	—
Net cash used in operating activities - continuing operations	(33,743)	(98,986)	(198,207)
Net cash provided by operating activities - discontinued operations	6,963	57,920	26,343
Net cash used in operating activities	(26,780)	(41,066)	(171,864)
Cash flows from investing activities:			
Purchases of investment debt securities	(552,737)	(349,457)	(330,713)
Sales and maturities of investment debt securities	451,921	420,580	497,421
Purchases of equipment, leasehold improvements, and furniture and fixtures	(568)	(397)	(3,891)
Net cash (used in) provided by investing activities - continuing operations	(101,384)	70,726	162,817
Net cash provided by investing activities - discontinued operations	363,233	—	—
Net cash provided by investing activities	261,849	70,726	162,817
Cash flows from financing activities:			
Payments for repurchases of convertible senior notes	(268,408)	57	—
Proceeds from exercise of options, net	1,684	18	1,301
Payments of debt issuance costs	(35)	—	—
Payments of employee withholding taxes related to stock-based awards	(557)	(1,737)	(1,994)
Payments for repurchase of common stock	—	(75,825)	—
Proceeds from issuance of Notes, net of debt issuance costs	—	116,734	—
Proceeds from terminations of capped call options	—	(38,129)	—
Net cash (used in) provided by financing activities - continuing operations	(267,316)	1,118	(693)
Net cash (used in) provided by financing activities - discontinued operations	—	—	—
Net cash (used in) provided by financing activities	(267,316)	1,118	(693)
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(6,302)	(2,023)	614
Net (decrease) increase in cash, cash equivalents and restricted cash	(38,549)	28,755	(9,126)
Cash, cash equivalents and restricted cash at beginning of period	94,409	65,654	74,780
Cash, cash equivalents and restricted cash at end of period	55,860	94,409	65,654
Less: Cash, cash equivalents and restricted cash of discontinued operations	—	1,581	1,710

Cash, cash equivalents and restricted cash of continuing operations	$ 55,860	$ 92,828	$ 63,944
Supplemental disclosure of non-cash transactions:			
Right-of-use asset obtained in exchange for new operating lease obligations	$ 5,749	$ —	$ —
Non-cash investing and financing activities			
Net increase in accrued fixed assets	130	—	—
Reconciliation of cash, cash equivalents and restricted cash included in the consolidated balance sheets:			
Cash and cash equivalents	$ 50,517	$ 84,709	$ 58,151
Restricted cash	5,343	8,119	5,793
Total cash, cash equivalents and restricted cash	$ 55,860	$ 92,828	$ 63,944
Supplemental non-cash disclosure:			
Issuance of common stock to noteholders in connection with repurchase of convertible notes	209,391	—	—
Exchange for existing 2023 and 2026 convertible notes	—	(421,200)	—
Exchange for new 2026 secured convertible notes	—	382,400	—
Issuance of common stock to financial advisor in connection with convertible notes exchange	—	10,000	—
Recognition of conversion option upon issuance of 2026 secured convertible notes	—	150,704	—
Extinguishment of conversion options upon exchange and repurchase of 2023 convertible notes and exchange of 2026 convertible notes	—	(39,146)	—
Supplementary cash flow data:			
Income taxes paid	5,051	—	—

See accompanying notes to consolidated financial statements

1. Overview of Business

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

On May 5, 2022, the Company entered into a series of agreements to sell the Company's ex-U.S. commercial operations and sublicense the right to commercialize Ocaliva for PBC and, if approved, OCA for NASH outside of the United States to Advanz Pharma and its affiliates (collectively, "Advanz") (the "Disposition Transaction"). Consideration under the agreements totaled $405 million up front, subject to adjustments including for cash, working capital, and assumed liabilities. On July 1, 2022, the Company completed the Disposition Transaction.

The Company is entitled to receive an additional $45 million from Advanz contingent upon receipt of extensions of orphan exclusivity for Ocaliva from the European Medicines Agency ("EMA") and Medicines and Healthcare products Regulatory Agency ("MHRA").

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

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

Use of Estimates

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

Reclassifications

Certain amounts in prior periods have been reclassified to reflect the impact of the discontinued operations treatment in order to conform to the current period presentation. See Note 3.

Foreign Currency

The Company's functional and reporting currency is the U.S. dollar. Transactions in foreign currencies are recorded at the exchange rate prevailing on the date of the transaction. The resulting monetary assets and liabilities are translated into U.S. dollars at exchange rates prevailing on the subsequent balance sheet date. Revenue and expense components are translated to U.S. dollars at weighted-average exchange rates in effect during the period. Foreign currency transaction gains and losses resulting from remeasurement are recognized in Other income, net within the consolidated statements of operations. Gains and losses as a result of foreign currency translation adjustments are recorded as a component of Accumulated other comprehensive loss, net in the stockholders' equity (deficit) section of the consolidated balance sheets and as Foreign currency translation gains (losses) within the accompanying consolidated statements of comprehensive income (loss).

Cash and Cash Equivalents

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

Restricted Cash

Restricted cash relates to short-term bank guarantees which provide financial assurance that the Company will fulfill certain customer obligations entered into in the normal course of business. The cash is restricted as to withdrawal or use while the related bank guarantee in favor of the customer remains outstanding.

Investment Debt Securities, Available-For-Sale

Investment debt securities are considered to be available-for-sale and are carried at fair market value. The estimated fair value of the available-for-sale investment debt securities is determined based on quoted market prices or rates for similar instruments. Unrealized gains and losses, if any, are reported in accumulated other comprehensive income (loss). The cost of investment debt securities is adjusted for amortization of premiums and accretion of discounts to maturity, which is included in Other income, net within the consolidated statements of operations. Realized gains and losses, interest and dividends on available-for-sale securities are also included in Other income, net.

Fair Value of Financial Instruments

The carrying amounts of certain financial instruments, including cash and cash equivalents, restricted cash, accounts receivable, prepaid expenses and other current assets, accounts payable, accrued expenses and other liabilities approximate fair value due to their short-term maturities.

Accounts Receivable

The Company extends credit to customers based on its evaluation of the customer's financial condition. The Company records receivables for all billings when amounts are due under standard terms. Accounts receivable are stated at amounts due net of applicable prompt pay discounts and other contractual adjustments as well as an allowance for doubtful accounts. The Company will write off accounts receivable when the Company determines that they are uncollectible.

Credit Losses

The allowance for credit losses is based on the Company's assessment of the collectibility of customer accounts. The Company regularly reviews the allowance by considering factors such as historical experience, the aging of the accounts receivable balances, credit conditions that may affect a customer's ability to pay, current and forecast economic conditions and other relevant factors.

The following table summarizes the allowance for credit losses activity on the Company's trade receivables for the year ended December 31, 2022 (in thousands):

Balance at December 31, 2021	$	58
Provision for credit losses		(4)
Write-offs		—
Balance at December 31, 2022	$	54

For available-for-sale investment debt securities in an unrealized loss position, the Company first assesses whether it intends to sell the security or it is more likely than not that it will be required to sell the security before recovery of its

amortized cost basis. If either of the criteria regarding intent or requirement to sell is met, the amortized cost basis is written down to fair value through income. For any investment debt securities that do not meet the criteria, the Company evaluates whether the decline in fair value has resulted from credit losses or other factors. Management considers the extent in which the fair value of the security is less than amortized costs, any changes to the rating of the security by a rating agency, changes in interest rates, and any other adverse factors related to the security. If the assessment indicates a credit loss, the present value of cash flows expected to be collected are compared to the amortized cost basis of the security. If the expected present value of cash flows is less than the amortized cost basis, a credit loss exists and an allowance for credit losses is recorded, limited to the amount that the fair value is below the amortized cost basis. Any impairment not recorded through an allowance is recognized in Other comprehensive income (loss).

Changes in the allowance for credit losses are recorded as a provision for (or reversal of) credit loss expense. Losses are charged against the allowance when management believes the uncollectibility of the security is confirmed or whether either of the criteria regarding intent or requirement to sell is met.

The Company excludes accrued interest from both the fair value and amortized cost basis in the assessment of credit losses on its available-for-sale investment debt securities and will instead elect to write-off any uncollectible accrued interest receivable balances in a timely manner, which is defined by the Company as when interest due becomes 90 days delinquent.

Concentration of Credit Risk

Financial instruments, which potentially subject the Company to concentrations of credit risk, principally consist of cash, cash equivalents, investment debt securities and accounts receivables from customers.

The Company currently invests its excess cash primarily in money market funds, and high quality, marketable debt instruments of corporations, financial institutions and government sponsored enterprises. The Company has adopted an investment policy that includes guidelines relative to credit quality, diversification and maturities to preserve principal and liquidity.

On a consolidated basis, for the year ended December 31, 2022, the Company's two largest customers (as defined below under "Revenue Recognition") accounted for 50% and 43% of the Company's net product sales, respectively. These two customers accounted for 45% and 42% of the Company's net product sales in 2021, and 42% and 41% of the Company's net product sales in 2020, respectively.

On a consolidated basis, the Company's two largest customers accounted for 45%, and 40% of the December 31, 2022 accounts receivable balance and 35% and 44% of the December 31, 2021 accounts receivable balance, respectively. The Company monitors its customers' financial credit worthiness in order to assess and respond to any changes in their credit profile.

Fixed Assets

Fixed assets are stated at cost, and depreciated over the estimated useful life of the assets. Depreciation is recorded using the straight-line method over the estimated useful lives of the respective assets, generally three to seven years. Leasehold improvements are amortized over the shorter of the asset's useful life or the life of the lease term. Expenditures for maintenance and repairs are charged to expense as incurred. Upon sale or retirement of assets, the cost of the assets disposed of and the related accumulated depreciation are removed from the consolidated balance sheets and any related gains or losses are reflected in the consolidated statements of operations.

Impairment of Long-Lived Assets

Long-lived assets consist of fixed assets and right-of-use ("ROU") assets. The Company evaluates long-lived assets for impairment when events and circumstances indicate that the carrying amount of an asset or group of assets may not be fully recoverable. If indicators of impairment exist, the Company assesses the recoverability of the affected long-lived assets by determining whether the carrying value of such assets can be recovered through undiscounted future operating cash flows. If the carrying amount is not recoverable, the Company measures the amount of any impairment by comparing the carrying value of the asset to the present value of the expected future cash flows associated with the use of the asset. There have been no impairments of any long-lived or ROU assets in the periods presented.

Inventory

Inventories are stated at the lower of cost or estimated realizable value. The Company determines the cost of inventory using the first-in, first-out (or FIFO) method. The Company capitalizes inventory costs associated with the Company's product after regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized; otherwise, such costs are expensed as research and development. The Company periodically analyzes its inventory levels to identify inventory that may expire prior to expected sale or has a cost basis in excess of its estimated realizable value, and writes-down such inventories as appropriate. In addition, the Company's product is subject to strict quality control and monitoring which the Company performs throughout the manufacturing process. If certain batches or units of product no longer meet quality specifications or become obsolete due to expiration, the Company records a charge to cost of sales to write down such unmarketable inventory to zero. No such charges were recorded in the years ended December 31, 2022, 2021 or 2020.

Leases

The Company determines if an arrangement is a lease at inception and records ROU assets and lease liabilities on the consolidated balance sheets at lease commencement based on the present value of remaining lease payments over the lease term. The Company only considers payments that are fixed and determinable at the time of commencement.

Operating lease liabilities are recognized based on the present value of the future minimum lease payments discounted by the Company's incremental borrowing rate. The Company measures ROU assets based on the corresponding lease liability adjusted for (i) payments made to the lessor at or before the commencement date, (ii) initial direct costs incurred and (iii) tenant incentives under the lease. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that it will exercise that option. Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term.

The Company has elected the practical expedient to exclude short-term leases from its ROU assets and lease liabilities; therefore leases with an initial term of 12 months or less are not recorded on the balance sheet. The Company recognizes lease expense for these leases on a straight-line basis over the lease term. The Company elected the practical expedient not to separate non-lease components from all leases. As the Company's leases do not provide an implicit rate, the Company uses an incremental borrowing rate based on the information available at the lease commencement date in determining the present value of the lease payments. The Company's incremental borrowing rate is the estimated rate that would be required to pay for a collateralized borrowing equal to the total lease payment over the lease term. The Company estimates its incremental borrowing rate based on an analysis of publicly traded debt securities of companies with credit and financial profiles similar to its own.

For short-term leases, the Company does not record ROU assets or lease liabilities, and records rent expense in its consolidated statements of operations on a straight-line basis over the lease term, with the exception of variable lease payments, which are expensed as incurred.

Discontinued Operations

Assets and liabilities of a group of components of an entity are classified as held for sale when all of the following criteria for a plan of sale have been met: (1) management, having the authority to approve the action, commits to a plan to sell the entities to be sold; (2) the entities to be sold are available for immediate sale, in their present condition, subject only to terms that are usual and customary for sales of such entities to be sold; (3) an active program to locate a buyer and other actions required to complete the plan to sell the entities have been initiated; (4) the sale of the entities is probable and is expected to be completed within one year; (5) the entities are being actively marketed for a price that is reasonable in relation to their current fair value; and (6) actions required to complete the plan indicate that it is unlikely that significant changes to the plan will be made or the plan will be withdrawn.

Components of an entity that are classified as held for sale and have operations and cash flows that can be clearly distinguished from the rest of the entity are required to be reported as assets and liabilities held for sale. A disposal of a group of components that is classified as held for sale is reported as discontinued operations if the disposal represents a strategic shift that has and will have a major effect on our operations and financial results.

In the period in which the components meet held-for-sale or discontinued operations criteria, the major current assets, other assets, current liabilities, and noncurrent liabilities shall be reported as components of total assets and liabilities separate from those balances of the continuing operations. Assets classified as held for sale are reported at the lower of their carrying value or fair value less costs to sell. Depreciation and amortization of assets ceases upon designation as held for sale. For components that meet the discontinued operations criteria, the results of operations for the discontinued operation are reclassified into separate line items in the consolidated statements of operations, net of income taxes for all periods presented.

Convertible Debt

The Company accounts for its convertible notes entirely as liabilities measured at amortized cost. As of December 31, 2021, the Company separately accounted for the liability (debt) and equity (conversion option) components of convertible debt instruments by allocating the proceeds from the issuance. The value assigned to the debt component was the estimated fair value, as of the issuance date, of a similar debt instrument without the conversion option. The amount of the equity component (and resulting debt discount) was calculated by deducting the fair value of the liability component from the principal amount of the convertible debt instrument. The resulting debt discount was amortized as additional non-cash interest expense over the expected life of the notes utilizing the effective interest method. For additional information, see Note 9 — Current and Long-Term Debt.

Revenue Recognition

Product Revenue, Net

The Company recognizes revenue upon delivery of Ocaliva to its customers. The Company provides the right of return to its customers for unopened product for a limited time before and after its expiration date. Returns are estimated based on historical experience and product shelf lives.

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

Rebates and Discounts

The Company contracts with the Centers for Medicare & Medicaid Services and other government agencies to make Ocaliva available to eligible patients. As a result, the Company estimates any rebates and discounts and deducts these estimated amounts from its gross product revenues at the time the revenues are recognized. The Company's estimates of rebates and discounts are based on the government mandated discounts, which are statutorily-defined and applicable to these government funded programs and assumptions developed using historical experience with actual payments and redemptions. The Company recorded $7.5 million and $6.7 million in such estimates as of December 31, 2022 and 2021, respectively, in accounts payable, accrued expenses and other liabilities on the consolidated balance sheets.

Other Incentives

Other incentives that the Company offers to indirect customers include co-pay assistance cards provided by the Company for PBC patients who reside in states that permit co-pay assistance programs. The Company's co-pay assistance program is intended to reduce each participating patient's portion of the financial responsibility for Ocaliva purchase price to a specified dollar amount. The Company estimates the amount of co-pay assistance provided to eligible patients based on the terms of the program when product is dispensed by the specialty pharmacies to the patients. These estimates are based on redemption information provided by third-party claims processing organizations. The Company recorded $2.0 million and $1.2 million in such estimates as of December 31, 2022 and 2021, respectively, in accounts payable, accrued expenses and other liabilities on the consolidated balance sheets.

Trade Allowances

The Company provides invoice discounts on Ocaliva sales to certain of its customers for prompt payment and records these discounts as a reduction to gross product revenues. These discounts are based on contractual terms. Trade allowances are recorded in accounts receivable, net of allowance for credit losses on the consolidated balance sheets.

Research and Development Expenses

Research and development costs that do not have alternative future use are charged to expense as incurred. This includes the cost of conducting clinical trials, compensation and related overhead for employees and consultants involved in research and development and the cost of the Company's manufacturing activities to supply ongoing and future clinical trials and preclinical studies. For periods prior to commercial launch, all manufacturing costs for OCA are expensed as research and development expenses. The Company will continue to incur manufacturing costs for OCA that are charged to research and development expenses for other indications such as NASH prior to their potential approval.

Stock-based Compensation

The Company accounts for stock-based compensation to employees, non-employee directors and non-employees granted share-based payments for services in accordance with ASC Topic 718, Compensation — Stock Compensation ("ASC 718"). The Company estimates the fair value of stock option awards using the Black-Scholes option pricing model on the date of the grant. Stock options granted to employees generally fully vest over four years and have a term of ten years. Restricted stock unit awards ("RSUs") and restricted stock awards ("RSAs") without a market condition are valued based on the closing price of the Company's common stock on the date of the grant. The fair value of time-based stock options and RSUs is recognized and amortized on a straight-line basis over the requisite service period of the award. The fair value of awards with market conditions is estimated using the Monte Carlo simulation method and expense is recognized on a straight-line basis over the requisite service period of the award. The Company accounts for all forfeitures when they occur.

Net Loss Per Share

Basic loss per share is computed by dividing net loss attributable to common stockholders (numerator) by the weighted average number of common shares outstanding (denominator) during the period. Potentially dilutive common shares include the shares of common stock issuable upon the exercise of outstanding stock options and unvested restricted stock units. The Company utilizes the control number concept in the computation of diluted earnings per share. The control number used is net loss from continuing operations. The control number requires that the same number of potentially dilutive securities applied in computing diluted earnings per share from continuing operations be applied to all other categories of income or loss. The Company accounts for the effect of the convertible notes on diluted net earnings per share using the if-converted method as they may be settled in cash or shares at the Company's option. Diluted net loss per share is the same as basic net loss per share, since the effects of potentially dilutive securities are antidilutive given net losses.

Income Taxes

The Company utilizes the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial statement carrying amounts and tax bases of assets and liabilities using enacted tax rates in effect for years in which the temporary differences are expected to reverse.

The Company determines the need for a valuation allowance by assessing the probability of realizing deferred tax assets. Judgment is required in making this assessment and to the extent future expectations change, the Company would have to assess the recoverability of its deferred assets at that time.

The Company's tax returns are subject to examination by U.S. Federal, state, and foreign taxing jurisdictions. The impact of an uncertain tax position taken or expected to be taken on an income tax return must be recognized in the financial statements at the largest amount that is more likely than not to be sustained. An uncertain income tax position will not be recognized in the financial statements unless it is more likely than not to be sustained.

Segments

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

Recently Adopted Accounting Pronouncements

In August 2020, the FASB issued ASU No. 2020-06, "Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity ("ASU 2020-06"), which simplifies the accounting for convertible instruments by eliminating the requirement to separately account for embedded conversion features as an equity component in certain circumstances. A convertible debt instrument will be reported as a single liability instrument with no separate accounting for an embedded conversion feature unless separate accounting is required for an embedded conversion feature as a derivative or under the substantial premium model. ASU 2020-06 simplifies the diluted earnings per share calculation by requiring that an entity use the if-converted method and that the effect of potential share settlement be included in diluted earnings per share calculations. Further, ASU 2020-06 requires enhanced disclosures about convertible instruments. The Company adopted ASU 2020-06 on January 1, 2022 using the modified retrospective method. Upon adoption at January 1, 2022, the Company made certain adjustments in its consolidated balance sheets which consisted of an increase of $176.3 million in Long-term debt, a net decrease of $307.4 million in Additional paid-in capital and a net decrease of $131.1 million in Accumulated deficit resulting from the reversal of previously recognized non-cash interest expense.

After adoption of ASU 2020-06, the Company now accounts for convertible notes entirely as liabilities measured at amortized cost. The Company did not elect the fair value option. Additionally, the Company will no longer incur non-cash interest expense for the amortization of debt discount related to the previously separated equity components. The Company will apply the if-converted methodology in computing diluted earnings per share if and when profitability is achieved.

The following table summarizes the adjustments made to the Company's consolidated balance sheet as of January 1, 2022 as a result of applying the modified retrospective method in adopting ASU 2020-06:

	As Reported December 31, 2021	ASU 2020-06 Adjustments	As Adjusted January 1, 2022
		(in thousands)	
Long-term debt	$ 539,782	$ 176,303	$ 716,085
Additional paid-in capital	$ 2,308,653	$ (307,371)	$ 2,001,282
Accumulated deficit	$ (2,489,772)	$ 131,068	$ (2,358,704)

3. Discontinued Operations

On May 5, 2022, the Company entered into the Disposition Transaction. Consideration under the agreements totaled $405 million up front, subject to adjustments for cash, working capital, and assumed liabilities. The Company is entitled to receive an additional cumulative $45 million from Advanz contingent upon receipt of extensions of orphan drug exclusivity from the EMA and MHRA. The Company will also receive royalties on any future net sales of OCA in NASH outside of the U.S., should Advanz obtain marketing authorization for this indication in ex-U.S. regions.

The Company continues to be responsible for the manufacturing and supply of OCA globally while Advanz is responsible for packaging, distribution and commercialization of the therapy in all markets outside of the U.S. In addition, the Company will be responsible for any difference between the cumulative rebate estimated for France for periods prior to July 1, 2022 and the amount agreed through final negotiations with the French government. Under the Transitional Service Agreement (the "TSA"), the Company agreed to provide certain transition services to Advanz for continuity purposes, and Advanz agreed to provide certain transition services to the Company for continuity purposes, including services with respect to human relations, finance, and information technology. The transition period for such services ended as of December 31, 2022. Under the Sublicense Agreement, the Company agreed to continue to conduct certain post-marketing work and other activities with respect to Ocaliva for PBC, including continuing to conduct certain PBC studies (the "PBC Post-Marketing Work"). Under the terms of the Sublicense Agreement, the Company will be reimbursed by Advanz for a portion of the total R&D costs related to the PBC Post-Marketing Work. The restricted cash presented on the consolidated balance sheets relates to the Company providing continuity of cash collateral that secures letters of credit issued for the benefit of former affiliates that were sold. Advanz currently compensates the Company via interest payments for providing this continuity of cash collateral for the letters of credit. It is expected that, at a later date, Advanz will deliver cash to the Company for 100% of the remaining cash collateral, which cash is to be then returned to Advanz following the release of funds by the financial institutions, and interest payments will cease.

On July 1, 2022, the Company completed the previously announced Disposition Transaction. As a result of this transaction, the Company's international business has been divested and its international commercial and medical infrastructure have transitioned to Advanz. Consideration totaled $405.0 million up front. Total cash consideration received upon closing was $366.5 million. Additional consideration of $38.5 million under the Share Purchase Agreement (the "SPA") was settled in connection with the completion statements (the post-closing statements completing and adjusting the flow of funds from the closing of the Disposition Transaction), which included adjustments for cash, working capital, and assumed liabilities. As part of the SPA settlement, the Company accrued for additional net consideration of $6.2 million to Advanz in Accounts payable, accrued expenses and other liabilities.

The Company recognized a gain of $369.3 million, net of income taxes on the sale of the ex-U.S. commercial operations upon closing.

Income for performing services under the TSA, recorded within Other income, net was $3.0 million for the year ended December 31, 2022. The total amount recognized as a reduction to Research & development expenses for a portion of the total R&D costs to be reimbursed by Advanz in relation to the PBC Post-Marketing Work was $5.4 million for the year ended December 31, 2022. Cash inflows were $7.0 million for the year ended December 31, 2022 under the TSA and PBC Post-Marketing Work.

Amounts applicable to the results of operations for the ex-U.S. commercial business in prior years have been recast to conform to the discontinued operations presentation. All amounts included in the notes to the audited consolidated financial statements relate to continuing operations unless otherwise noted.

The following table presents the carrying amounts of the classes of assets and liabilities related to the discontinued operations as of December 31, 2022 and December 31, 2021:

	December 31, 2022	December 31, 2021
Restricted cash	$ —	$ 1,581
Accounts receivable, net of allowance for credit losses	—	19,280
Prepaid expenses and other current assets	—	2,508
Fixed assets, net	—	96
Inventory	—	736
Security deposits	—	2,332
Other assets	—	2,562
Total assets classified as discontinued operations in consolidated balance sheets	$ —	$ 29,095
Accounts payable, accrued expenses and other liabilities	$ —	$ 54,436
Long-term other liabilities	—	1,344
Total liabilities classified as discontinued operations in consolidated balance sheets	$ —	$ 55,780

The Company maintains a full valuation allowance on the deferred tax assets related to discontinued operations at December 31, 2022 and 2021. The deferred tax assets primarily relate to foreign tax losses. The deferred tax assets before valuation allowance recorded in non-current assets of discontinued operations are $0.0 million and $22.7 million, respectively.

As of December 31, 2022, there were no assets or liabilities classified as held for sale.

The following table presents the results of operations related to the discontinued operations for the years ended December 31, 2022, 2021 and 2020 respectively:

	Year Ended December 31,		
	2022	2021	2020
Product revenue, net	$ 58,065	$ 102,718	$ 78,720
Cost of sales	1,234	1,895	2,969
Selling, general and administrative	28,356	53,367	71,991
Research and development	1,093	2,525	2,456
Restructuring	—	198	2,817
Other (expense) income, net	(9)	193	33
Income (loss) from discontinued operations	$ 27,373	$ 44,926	$ (1,480)
Gain on the sale of the ex-U.S. commercial operations and sublicense	377,301	—	—
Income (loss) from discontinued operations, pre-tax	$ 404,674	$ 44,926	$ (1,480)
Income tax expense	(8,000)	—	—
Income (loss) from discontinued operations, net of tax	$ 396,674	$ 44,926	$ (1,480)

The income tax expense has been recorded within discontinued operations as it relates to the income tax impact on the sale of the international business to Advanz. The Company expects to utilize net operating loss carryforwards ("NOLs") to offset the income tax impact on the sale, however, primarily due to limitations on the amount of NOLs which can be used, the Company recorded an income tax provision in the United Kingdom and certain U.S. state jurisdictions of $6.5 million and $1.5 million, respectively.

Stock-based compensation expense recognized under discontinued operations, included in net income from discontinued operations, was $4.5 million, $5.9 million and $10.7 million for the years ended December 31, 2022, 2021 and 2020, respectively.

The Company modified certain stock option, stock grant and stock-based awards to accelerate vesting in anticipation of the sale of the ex-U.S. commercial operations to Advanz. The Company accelerated the vesting of all awards held by employees of those operations being sold. As a result, incremental compensation expense of $3.4 million was recognized in discontinued operations based on the fair value of the modified awards for the year ended December 31, 2022.

The following table presents the calculation of the gain on sale related to the discontinued operations for the year ended December 31, 2022.

	Year Ended December 31, 2022
Proceeds from sale of business	$ 366,500
Transaction costs	(10,193)
Carrying value of net liabilities sold	27,043
Working capital adjustments	(11,012)
Release of accumulated currency translation adjustments for disposed subsidiaries	7,319
Supply & manufacturing agreement liability	(2,356)
Gain on sale, pre-tax	377,301
Income tax expense	(8,000)
Gain on sale, net of tax	$ 369,301

The following table presents the net cash provided by operating and investing activities for the assets and liabilities classified as discontinued operations for the years ended December 31, 2022, 2021 and 2020 respectively:

	Year Ended December 31,		
	2022	2021	2020
Net income (loss) from discontinued operations	$ 396,674	$44,926	$(1,480)
Adjustment of non-cash activities	5,044	7,149	12,892
Decrease (increase) in accounts receivable	18,637	(3,721)	(872)
Decrease in prepaid expenses and other current assets	2,431	1,251	85
Decrease (increase) in inventory	692	(147)	(475)
Decrease in security deposits	2,252	—	(14)
Decrease in operating lease liabilities	(386)	(1,083)	(931)
Decrease (increase) in other assets	2,115	20	(138)
(Decrease) increase in accounts payable, accrued expenses and other current liabilities	(53,069)	9,525	17,146
(Decrease) increase in long-term other liabilities	(964)	—	130
Decrease in fixed assets	37	—	—
Reclassification of cash proceeds from sale of business to investing activities	(366,500)	—	—
Net cash provided by operating activities	$ 6,963	$57,920	$26,343
Proceeds from sale of business, net of cash	363,233	—	—
Net cash provided by investing activities	$ 363,233	$ —	$ —

4. Cash, Cash Equivalents and Investments

The following table summarizes the Company's cash, cash equivalents and investments as of December 31, 2022 and 2021:

	As of December 31, 2022				
	Amortized Cost	Allowance for Credit Losses	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
			(in thousands)		
Cash and cash equivalents:					
Cash and money market funds	$ 50,517	$ —	$ —	$ —	$ 50,517
Total cash and cash equivalents	50,517	—	—	—	50,517
Investment debt securities:					
Commercial paper	102,379	—	7	(183)	102,203
Corporate debt securities	304,234	—	33	(1,390)	302,877
U.S. government agency bonds	24,100	—	4	(109)	23,995
U.S. Treasury securities	5,993	—	—	(19)	5,974
Total investment debt securities	436,706	—	44	(1,701)	435,049
Total cash, cash equivalents and investment debt securities	$ 487,223	$ —	$ 44	$ (1,701)	$ 485,566

	As of December 31, 2021				
	Amortized Cost	Allowance for Credit Losses	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
			(in thousands)		
Cash and cash equivalents:					
Cash and money market funds	$ 76,709	$ —	$ —	$ —	$ 76,709
Commercial paper	8,000	—	—	—	8,000
Total cash and cash equivalents	84,709	—	—	—	84,709
Investment debt securities:					
Commercial paper	84,513	—	—	(49)	84,464
Corporate debt securities	232,721	—	16	(245)	232,492
Municipal bonds	5,028	—	—	(1)	5,027
U.S. Treasury securities	12,998	—	—	(1)	12,997
Total investment debt securities	335,260	—	16	(296)	334,980
Total cash, cash equivalents and investment debt securities	$ 419,969	$ —	$ 16	$ (296)	$ 419,689

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

	As of December 31, 2022					
	Less than 12 months		12 months or longer		Total	
	(in thousands)					
	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses
Commercial paper	$ 93,659	$ (183)	$ —	$ —	$ 93,659	$ (183)
Corporate debt securities	256,918	(1,174)	27,494	(216)	284,412	(1,390)
U.S. government agency bonds	17,866	(109)	—	—	17,866	(109)
U.S. Treasury securities	5,974	(19)	—	—	5,974	(19)
Total	$ 374,417	$ (1,485)	$ 27,494	$ (216)	$ 401,911	$ (1,701)

	As of December 31, 2021					
	Less than 12 months		12 months or longer		Total	
	(in thousands)					
	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses
Commercial paper	$ 81,464	$ (49)	$ —	$ —	$ 81,464	$ (49)
Corporate debt securities	196,120	(245)	—	—	196,120	(245)
Municipal bonds	5,027	(1)	—	—	5,027	(1)
U.S. Treasury securities	12,997	(1)	—	—	12,997	(1)
Total	$ 295,608	$ (296)	$ —	$ —	$ 295,608	$ (296)

At December 31, 2022 and 2021, the Company had 122 and 97 available-for-sale investment debt securities, respectively in an unrealized loss position without an allowance for credit losses. Unrealized losses on corporate debt securities have not been recognized into income because the issuers' bonds are of high credit quality (rated A3/A- or higher), management does not intend to sell and it is likely that management will not be required to sell the securities prior to their anticipated recovery and the decline in fair value is largely due to market conditions and/or changes in interest rates. The issuers continue to make timely interest payments on the bonds. The fair value is expected to recover as the bonds approach maturity. For the years ended December 31, 2022 and 2021, no allowance was recorded for credit losses.

Accrued interest receivable on available-for-sale investment debt securities totaled $2.4 million and $1.3 million at December 31, 2022 and December 31, 2021, respectively, is excluded from the estimate of credit losses and is included in Prepaid expenses and other current assets.

5. Fair Value Measurements

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

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

- Unadjusted Quoted Prices — The fair value of an asset or liability is based on unadjusted quoted prices in active markets for identical assets or liabilities (Level 1).

- Pricing Models with Significant Observable Inputs — The fair value of an asset or liability is based on information derived from either an active market quoted price, which may require further adjustment

based on the attributes of the financial asset or liability being measured, or an inactive market transaction (Level 2).

- Pricing Models with Significant Unobservable Inputs — The fair value of an asset or liability is primarily based on internally derived assumptions surrounding the timing and amount of expected cash flows for the financial instrument. Therefore, these assumptions are unobservable in either an active or inactive market (Level 3).

The Company considers an active market as one in which transactions for the asset or liability occur with sufficient frequency and volume to provide pricing information on an ongoing basis. Conversely, the Company views an inactive market as one in which there are few transactions for the asset or liability, the prices are not current, or price quotations vary substantially either over time or among market makers. Where appropriate, non-performance risk, or that of a counterparty, is considered in determining the fair values of liabilities and assets, respectively.

The Company's cash deposits, money market funds and U.S Treasury securities are classified within Level 1 of the fair value hierarchy because they are valued using bank balances or quoted market prices from active markets. Investment debt securities are classified as Level 2 instruments based on market pricing and other observable inputs.

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

		Fair Value Measurements Using		
	Total	Level 1	Level 2	Level 3
		(in thousands)		
December 31, 2022				
Assets				
Cash and cash equivalents:				
Money market funds	$ 27,035	$ 27,035	$ —	$ —
Available-for-sale investment debt securities:				
Commercial paper	102,203	—	102,203	—
Corporate debt securities	302,877	—	302,877	—
U.S. government agency bonds	23,995	—	23,995	—
U.S. Treasury securities	5,974	5,974	—	—
Total financial assets	$ 462,084	$ 33,009	$ 429,075	$ —
December 31, 2021				
Assets				
Cash and cash equivalents:				
Money market funds	$ 39,287	$ 39,287	$ —	$ —
Commercial paper	8,000	—	8,000	—
Available-for-sale investment debt securities:				
Commercial paper	84,464	—	84,464	—
Corporate debt securities	232,492	—	232,492	—
Municipal bonds	5,027	—	5,027	—
U.S. Treasury securities	12,997	12,997	—	—
Total financial assets	$ 382,267	$ 52,284	$ 329,983	$ —

See Note 9 for the carrying amounts and estimated fair values of the Company's 3.50% Convertible Senior Secured Notes due 2026 ("2026 Convertible Secured Notes"), 2.00% Convertible Senior Notes due 2026 ("2026 Convertible Notes") and 3.25% Convertible Senior Notes due 2023 ("2023 Convertible Notes").

The gross realized gains and losses on sales of available-for-sale investment debt securities were not material for the fiscal years ended December 31, 2022, 2021, and 2020.

The aggregate fair value of all available-for-sale investment debt securities (commercial paper, corporate debt securities, U.S. government agency bonds, municipal bonds and U.S. Treasury securities), by contractual maturity, are as follows:

	Fair Value as of	
	December 31, 2022	December 31, 2021
	(in thousands)	
Due in one year or less	$ 391,488	$ 305,914
Due after one year through two years	43,561	29,066
Total investment debt securities	$ 435,049	$ 334,980

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

6. Fixed Assets, Net

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

	Useful lives (Years)	December 31, 2022	December 31, 2021
		(in thousands)	
Office equipment and software	3	$ 3,112	$ 4,751
Leasehold improvements	Shorter of remaining lease term or useful life	395	12,884
Furniture and fixtures	7	1,280	3,772
Subtotal		4,787	21,407
Less: accumulated depreciation		(3,800)	(18,126)
Fixed assets, net		$ 987	$ 3,281

Depreciation expense for the years ended December 31, 2022, 2021 and 2020 was approximately $3.0 million, $2.8 million and $2.9 million, respectively.

7. Inventory

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

	December 31, 2022	December 31, 2021
	(in thousands)	
Work-in-process	$ 6,230	$ 7,801
Finished goods	232	82
Inventory	$ 6,462	$ 7,883

8. Accounts Payable, Accrued Expenses and Other Liabilities

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

	December 31, 2022	December 31, 2021
	(in thousands)	
Accounts payable	$ 14,234	$ 17,598
Accrued employee compensation	24,737	20,845
Accrued contracted services	58,875	51,136
Accrued rebates, returns, discounts and other incentives	14,460	11,626
Accrued income taxes payable	3,144	—
Other liabilities	1,527	2,575
Accounts payable, accrued expenses and other liabilities	$ 116,977	$ 103,780

Research & Development Tax Credit

The Company has benefited from the U.K. Small and Medium-sized Enterprise R&D Tax Credit scheme, or the SME scheme, under which it can obtain a tax credit of up to 33.4% of eligible research and development expenses incurred by the Company in the U.K. Eligible expenses generally include employment costs for research staff, consumables, software and certain internal overhead costs incurred as part of research projects.

The Company has also started to recently benefit from the U.K. Research and Development Expenditure Scheme, or the RDEC scheme, under which it can obtain a tax credit of 12% of eligible research and development expenses incurred by the Company in the U.K. The RDEC scheme is more restrictive than the SME scheme, and generally applies where qualifying R&D expenditure is not eligible for relief under the SME scheme.

The Company has submitted claims seeking to obtain tax credits for qualifying R&D expenses incurred in the 2015, 2016, 2017, 2018, 2019 and 2020 calendar years. As described further in Note 12, the 2018 SME claim was finalized during the quarter ended June 30, 2022, and therefore the $4.0 million payment received in June 2021, which was previously deferred, was released into income as a reduction to Research & development expenses.

With respect to the 2019 RDEC claim, in February 2022, the Company received a payment of $3.8 million from His Majesty's Revenue and Customs (the "HMRC"), the U.K.'s government tax authority. Given the claim review has not been finalized for the 2019 year, the $3.8 million credit received, which has been reduced by $0.3 million due to foreign currency translation is recorded as a deferred liability within Accounts payable, accrued expenses and other liabilities.

9. Current and Long-Term Debt

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

	December 31, 2022				
	2026 Convertible Secured Notes	2026 Convertible Notes	2023 Convertible Notes	Total Current Portion of Long-Term Debt	Total Long-Term Debt
			(in thousands)		
Liability component					
Principal	$ 111,143	$ 115,349	$ 109,808	$ 109,808	$ 226,492
Unamortized debt issuance costs	(1,728)	(1,660)	(239)	(239)	(3,388)
Net carrying amount	$ 109,415	$ 113,689	$ 109,569	$ 109,569	$ 223,104

	December 31, 2021				
	2026 Convertible Secured Notes	2026 Convertible Notes	2023 Convertible Notes	Total Current Portion of Long-Term Debt	Total Long-Term Debt
			(in thousands)		
Liability component					
Principal	$ 500,000	$ 115,349	$ 113,655	$ —	$ 729,004
Unamortized debt issuance costs	(7,132)	(2,313)	(816)	—	(10,261)
Unamortized debt discount	(141,303)	(30,228)	(7,430)	—	(178,961)
Net carrying amount	$ 351,565	$ 82,808	$ 105,409	$ —	$ 539,782
Equity component, net of issuance costs*	$ 147,458	$ 62,841	$ 97,072		

* Recorded as a reduction of Additional paid-in capital upon the adoption of ASU 2020-06.

The Company has three series of convertible notes outstanding (together, the "Convertible Notes"). All three series are convertible under certain circumstances into cash, shares of the Company's common stock, or a combination thereof, at the Company's election.

The 2023 Convertible Notes were issued on July 6, 2016, in the amount of $460.0 million principal, at an interest rate of 3.25%. The Company received net proceeds from their sale of $447.6 million, net of $12.4 million in underwriting discounts, commissions, and estimated offering expenses.

The 2026 Convertible Notes were issued on May 14, 2019, in the amount of $230.0 million principal, at an interest rate of 2.00%. The Company received net proceeds from their sale of $223.4 million, net of $6.6 million in underwriting discounts, commissions, and estimated offering expenses.

2021 Exchange of 2023 and 2026 Convertible Notes and Sale of 2026 Convertible Secured Notes

On August 10, 2021, the Company entered into privately negotiated exchange and subscription agreements with a limited number of existing "accredited investors" and "qualified institutional buyers" (as defined under Securities Act rules) holding 2023 Convertible Notes and 2026 Convertible Notes to (1) exchange $306.5 million principal of 2023

Convertible Notes for $292.4 million principal of new notes, (2) exchange $114.7 million principal of 2026 Convertible Notes for $90.0 million principal of new notes, and (3) sell $117.6 million principal of new notes for cash. On August 17, 2021, these new notes were issued as 2026 Convertible Secured Notes in the amount of $500.0 million principal, at an interest rate of 3.50%. The Company received cash proceeds from the sale of notes of approximately $116.7 million, net of $0.9 million in issuance costs. The Company also paid its financial advisor $10.0 million in stock for services rendered, in the amount of 769,823 shares, based on the closing price of $12.99 per share on August 20, 2021.

2021 Repurchase of 2023 Convertible Notes

Further, on September 9, 2021, the Company entered into privately negotiated agreements with certain holders of 2023 Convertible Notes to repurchase $39.9 million principal for $38.1 million in cash, which purchase closed on September 14, 2021.

The 2021 repurchases of the 2023 Convertible Notes and 2026 Convertible Secured Notes were all treated as extinguishments of debt.

	Gain on extinguishment of debt	Reduction to additional paid-in capital
	(in thousands)	
Exchange of 2023 Convertible Notes	$ 2,169	$ 14,139
Exchange of 2026 Convertible Notes	13,839	23,074
Repurchase of 2023 Convertible Notes	503	1,933
Total	$ 16,511	$ 39,146

2022 Repurchase of 2023 Convertible Notes

On June 1, 2022, the Company entered into an agreement with a certain holder of 2023 Convertible Notes to repurchase $3.8 million principal for $3.8 million in cash, which purchase closed on June 3, 2022.

2022 Repurchases of 2026 Convertible Secured Notes

On August 18, September 1, and September 6, 2022, the Company entered into privately negotiated agreements to repurchase $327.9 million, $44.5 million, and $9.3 million of 2026 Convertible Secured Notes, using a combination of cash and equity, which purchases closed on August 25, September 6, and September 8, 2022, respectively.

The Company exchanged the existing 2026 Convertible Secured Notes for $222.0 million, $22.7 million, and $5.2 million in cash, respectively, and 9,358,269, 1,653,130, and 318,000 shares, respectively, of newly issued common stock, par value $0.001 per share.

Based on the Company's closing stock price on the dates of the agreements of $19.70, $18.06, and $16.32, respectively, the shares were worth $184.4 million, $29.9 million, and $5.2 million, respectively.

On September 9, 2022, the Company entered into a privately negotiated agreement to repurchase $7.1 million of 2026 Convertible Secured Notes using cash, which purchase closed on September 19, 2022. The Company exchanged the existing 2026 Convertible Secured Notes for $8.2 million in cash.

The 2022 repurchases of the 2023 Convertible Notes and 2026 Convertible Secured Notes were all treated as extinguishments of debt.

	(Loss) gain on extinguishment of debt, net	Net reduction to long-term debt
	(in thousands)	
Repurchase of 2023 Convertible Notes	$ 21	$ 3,829
Repurchase of 2026 Convertible Secured Notes	(91,799)	382,191
Total	$ (91,778)	$ 386,020

Net of these transactions, as of December 31, 2022, the Company has $336.3 million in gross current and long-term debt, as shown in the table further above.

Fair Value

The approximate fair value of the Convertible Notes was determined as follows using Level 2 inputs based on quoted market values:

	December 31, 2022	December 31, 2021
	(in thousands)	
2026 Convertible Secured Notes	$ 108,012	$ 543,370
2026 Convertible Notes	$ 87,307	$ 69,492
2023 Convertible Notes	$ 107,680	$ 107,727

The Note Indentures

The 2023 Convertible Notes, and the 2026 Convertible Notes, were each issued pursuant to a Base Indenture, dated as of July 6, 2016, between the Company and U.S. Bank National Association ("U.S. Bank"), as trustee, and a First Supplemental Indenture (with respect to the 2023 Convertible Notes) and Second Supplemental Indenture (with respect to the 2026 Convertible Notes), dated July 6, 2016, and May 14, 2019, respectively, each between the Company and U.S. Bank as trustee. The 2026 Convertible Secured Notes were issued pursuant to a Base Indenture and a First Supplemental Indenture, each dated as of August 17, 2021, between the Company and U.S. Bank as trustee and collateral agent. In connection with the issuance of the 2026 Convertible Secured Notes, the Company also entered into a Security Agreement, dated as of August 17, 2021, with U.S. Bank as collateral agent.

Pursuant to these indentures, the 2023 Convertible Notes and 2026 Convertible Notes are senior unsecured obligations, and the 2026 Convertible Secured Notes are senior secured obligations, of the Company. Each indenture provides for customary events of default.

Each series of notes bears a fixed rate of interest as identified above, payable semi-annually in arrears:

		Semi-annual payment dates		
	First payment date	First	Second	Maturity date*
2026 Convertible Secured Notes	February 15, 2022	February 15	August 15	February 15, 2026
2026 Convertible Notes	November 15, 2019	May 15	November 15	May 15, 2026
2023 Convertible Notes	January 1, 2017	January 1	July 1	July 1, 2023

* Unless earlier repurchased, redeemed, or converted.

Each of the three series of notes is convertible under certain circumstances. Prior to January 1, 2023 (for the 2023 Convertible Notes), February 15, 2026 (for the 2026 Convertible Notes), and November 15, 2025 (for the 2026 Convertible Secured Notes), holders may convert their notes only under any of the following circumstances:

(i) During any calendar quarter commencing after the calendar quarter ended on September 30, 2016 (for the 2023 Convertible Notes), June 30, 2019 (for the 2026 Convertible Notes), or December 31, 2021 (for the 2026 Convertible Secured Notes), if the last reported sale price of the Company's common stock for at least 20 trading days (whether or not consecutive) during the period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is at least 130% of the applicable conversion price (as defined in the applicable indenture) on each applicable trading day (the "Stock Price Conversion Condition").

(ii) During the five business day period after any five consecutive trading day period in which the trading price (as defined in the applicable indenture) per $1,000 principal amount for each trading day was less than 98% of the product of the last reported sale price of the Company's common stock and the applicable conversion rate (as defined in the applicable indenture) on each such trading day.

(iii) If the Company calls any or all of the applicable series of notes for redemption, at any time prior to the close of business on the scheduled trading day immediately preceding the redemption date.

(iv) Upon the occurrence of specified corporate events.

After those dates, holders may convert their notes, regardless of the foregoing circumstances, at any time until immediately preceding the applicable maturity date.

Upon conversion of notes, the Company will pay or deliver cash, shares of common stock (or cash in lieu of fractional shares), or a combination of cash and common stock, at the Company's election.

The initial conversion rates of the Convertible Notes per $1,000 principal amount, and the approximate conversion price, are as follows:

	Initial conversion rate	Approximate conversion price
2026 Convertible Secured Notes	47.7612	$20.94
2026 Convertible Notes	9.2123	$108.55
2023 Convertible Notes	5.0358	$198.58

These conversion rates are subject to adjustment upon occurrence of certain events but will not be adjusted for accrued and unpaid interest. Also, if certain specified events occur, the conversion rate will be increased for notes converted in connection with such events.

The Convertible Notes are redeemable by the Company in certain circumstances starting July 6, 2021 (for the 2023 Convertible Notes), May 20, 2023 (for the 2026 Convertible Notes), and February 20, 2024 (for the 2026 Convertible Secured Notes). After such dates, the Company may redeem for cash all or any part of the applicable Convertible Notes, at its option, if the last reported sale price of the common stock has been at least 130% of the applicable conversion price then in effect for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading day period ending on and including the trading day immediately preceding the date of the applicable notice of redemption. The redemption price is equal to 100% of the principal amount redeemed, plus accrued and unpaid interest to (but excluding) the redemption date.

No sinking fund is provided for any of the Convertible Notes.

If the Company undergoes a fundamental change (as defined in the applicable indenture), noteholders may require the Company 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.

Upon the occurrence of certain corporate events (i.e., a "make-whole fundamental change", as defined in the applicable indenture), the Company will, under certain circumstances, increase the conversion rate for holders of the Convertible Notes who elect to convert in connection with such corporate events. In addition, with respect to the 2026 Convertible Secured Notes, (1) if the Company elects to redeem all or part of such notes and provides notice of redemption to the holders or (2) if the Stock Price Conversion Condition is satisfied with respect to any calendar quarter commencing after the quarter ended September 30, 2022, the Company will, under certain circumstances, increase the conversion rate for holders who elect to convert (1) during the related redemption period, or (2) in connection with such Stock Price Conversion Condition. Upon a Company redemption of the 2026 Convertible Secured Notes, holders of notes called for redemption may be eligible to receive a make-whole premium. The Company, at its option, will satisfy the conversion obligation through cash, shares of common stock, or a combination of cash and common stock. The right to redeem the 2026 Convertible Secured Notes requires the Company to specify a date of redemption no earlier than 60 days and no later than 90 days after the notice of redemption is sent. If a holder elects to convert its 2026 Convertible Secured Notes prior to the effective date of a make-whole fundamental change or the date of the redemption notice, then it is not entitled to the increased conversion rate in connection with such make-whole fundamental change or redemption.

Upon certain events of default occurring and continuing, either the indenture trustee or holders of at least 25% in aggregate principal amount of a series of notes then outstanding may declare the entire principal amount of that series of notes, and accrued interest, if any, to be immediately due and payable. Upon events of default involving specified bankruptcy events involving the Company, the Convertible Notes are due and payable immediately.

The 2026 Convertible Secured Notes indenture and security agreement include (1) customary covenants, (2) guarantor provisions, and (3) collateral provisions. The 2026 Convertible Secured Notes may become guaranteed in the future by subsidiaries of the Company that meet certain threshold requirements, with the 2026 Convertible Secured Notes becoming senior obligations of such guarantor. The 2026 Convertible Secured Notes are secured by a first priority security interest in substantially all assets of the Company, and of any guarantors, subject to certain exceptions.

The Capped Call Transactions

On June 30, 2016, in connection with the pricing of the 2023 Convertible Notes, the Company entered into privately-negotiated capped call agreements (the "Base Capped Calls") with each of Royal Bank of Canada, UBS AG, London Branch, and Credit Suisse Capital LLC. On July 1, 2016, in connection with the underwriters' exercise of their over-allotment option in full, the Company entered into additional capped call agreements (the "Additional Capped Calls" and, together with the Base Capped Calls, the "Capped Calls") with same counterparties.

The Capped Calls are considered to be instruments indexed to the Company's own shares and met the criteria to be classified within equity. Therefore, they are not remeasured.

In August 2021, in connection with the exchange of 2023 Convertible Notes, of the 460,000 Capped Call options outstanding (400,000 Base Capped Call options and 60,000 Additional Capped Call Options), 306,486 options were terminated (246,486 Base Capped Call options and 60,000 Additional Capped Call options), equivalent to approximately 1.5 million shares.

In September 2021, in connection with the additional repurchase of $39.9 million of 2023 Convertible Notes, 39,859 additional Capped Call options were terminated, equivalent to approximately 0.2 million shares, with 113,655 Base Capped Call options remaining, equivalent to approximately 0.6 million shares.

Upon settlement of each termination, the Company received an immaterial amount in cash proceeds, which was recorded as an increase to additional paid-in capital.

Interest Expense on Convertible Notes

The table summarizes the total interest expense recognized in the periods presented:

	Year ended December 31, 2022			
	2026 Convertible Secured Notes	2026 Convertible Notes	2023 Convertible Notes	Total
		(in thousands)		
Contractual interest expense	$ 12,850	$ 2,308	$ 3,621	$ 18,779
Amortization of debt issuance costs	1,669	466	471	2,606
Accretion of debt discount	—	—	—	—
Total interest expense	$ 14,519	$ 2,774	$ 4,092	$ 21,385

	Year ended December 31, 2021			
	2026 Convertible Secured Notes	2026 Convertible Notes	2023 Convertible Notes	Total
		(in thousands)		
Contractual interest expense	$ 6,465	$ 3,766	$ 10,857	$ 21,088
Amortization of debt issuance costs	474	641	1,429	2,544
Accretion of debt discount	9,401	8,378	13,008	30,787
Total interest expense	$ 16,340	$ 12,785	$ 25,294	$ 54,419

	Year ended December 31, 2020			
	2026 Convertible Secured Notes	2026 Convertible Notes	2023 Convertible Notes	Total
		(in thousands)		
Contractual interest expense	$ —	$ 4,600	$ 14,950	$ 19,550
Amortization of debt issuance costs	—	717	1,823	2,540
Accretion of debt discount	—	9,371	16,593	25,964
Total interest expense	$ —	$ 14,688	$ 33,366	$ 48,054

The effective interest rates during the years ended December 31, 2022 for the 2026 Convertible Secured Notes, 2026 Convertible Notes and 2023 Convertible Notes are 4.03%, 2.44% and 3.69%, respectively. The effective interest rates during the year ended December 31, 2021 for the 2026 Convertible Secured Notes, 2026 Convertible Notes and 2023 Convertible Notes were 12.80%, 9.90% and 8.42%, respectively. The effective interest rates during the year ended December 31, 2020 for the 2026 Convertible Notes and 2023 Convertible Notes were 9.90% and 8.42%, respectively.

Accrued interest on the Convertible Notes was approximately $3.5 million and $8.6 million as of December 31, 2022 and 2021, respectively.

The Company's total recorded debt issuance costs are $8.7 million, which are being amortized using the effective interest method through the date of maturity. As of December 31, 2022, $0.2 million of debt issuance costs for the 2023 Convertible Notes are unamortized on the consolidated balance sheets in Current portion of long-term debt. As of December 31, 2022 and 2021, $3.4 million of debt issuance costs for the 2026 Convertible Secured Notes and 2026

Convertible Notes and $10.3 million of debt issuance costs for the 2026 Convertible Secured Notes, 2026 Convertible Notes and 2023 Convertible Notes, respectively, are unamortized on the consolidated balance sheets in Long-term debt.

Cash payments for interest were $23.8 million, $18.4 million and $19.6 million for the years ended December 31, 2022, 2021 and 2020, respectively.

10. Stockholders' Equity and Preferred Stock

Common Stock

As of December 31, 2022 and 2021, the Company had 90,000,000 authorized shares of common stock, par value $0.001 per share, respectively.

In connection with the note exchange transactions described in Note 9, on August 11, 2021, the Company completed a repurchase of 4,521,502 shares of its common stock for an aggregate cash cost of $75.8 million. The Company subsequently retired the shares of common stock. The Company's common stock is reduced by an amount equal to the number of shares repurchased multiplied by the par value of such shares. The excess amount that is repurchased over its par value is allocated as a reduction to additional paid-in capital. The Company also issued 769,823 shares to its financial advisor for services rendered, equivalent to $10.0 million. The financial advisory fee was allocated as debt or equity issuance costs in proportion to the allocation of the liability and equity components of the 2026 Convertible Secured Notes.

In August and September 2022, the Company exchanged the existing 2026 Convertible Secured Notes for an aggregate of 11,329,399 shares of newly issued common stock. The Company's common stock was increased by an amount equal to the number of shares issued multiplied by the par value of such shares. The excess amount that was issued over its par value was allocated as an increase to additional paid-in capital.

Dividends

Subject to preferences that may be applicable to any outstanding shares of preferred stock, holders of common stock are entitled to receive ratably such dividends, if any, as may be declared from time to time by the Company's board of directors out of funds legally available for dividend payments. The Company has never declared or paid any cash dividends on its common stock, and does not anticipate paying any cash dividends on its common stock in the foreseeable future. As part of the agreements for the 2026 Convertible Secured Notes, the Company is restricted from dividend payments. The Company intends to retain all available funds and any future earnings to fund the development and expansion of its business. Any future determination to pay dividends will be at the discretion of the board of directors and will depend upon a number of factors, including the results of operations, financial condition, future prospects, contractual restrictions, restrictions imposed by applicable law and other factors the board of directors deems relevant.

Voting

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

Preferred Stock

As of December 31, 2022 and 2021, the Company had 5,000,000 authorized shares of preferred stock, par value $0.001 per share, of which none are issued.

11. Stock Compensation

The Company's 2012 Equity Incentive Plan ("2012 Plan") became effective upon the pricing of its initial public offering in October 2012 (the "IPO").

On January 1, 2022, the number of shares available for issuance under the 2012 Plan increased by 1,182,918 as a result of the automatic increase provisions thereof.

In April 2022, the Company's Compensation Committee and Board of Directors approved the Company's Amended and Restated Equity Incentive Plan ("2022 Plan"), which became effective upon stockholder approval at the annual meeting of stockholders on May 25, 2022, and which replaced the Company's 2012 Plan. Under the 2022 Plan, the Company may grant stock options, which include incentive stock options ("ISOs") and non-qualified stock options ("NSOs"), stock grants, which include unrestricted shares, RSAs and performance restricted shares ("PSAs") along with stock-based awards, which include RSUs and performance restricted stock unit awards ("PRSUs"). The pool of available shares under the 2022 Plan consists of those shares which remained unallocated under the 2012 Plan, plus any shares subject to previously issued awards which are forfeited. The 2022 Plan does not contain an evergreen share replenishment clause and prohibits the repricing of stock options. The 2022 Plan will remain effective for a ten-year term, expiring in 2032. The 2022 Plan does not included an evergreen share replenishment provision.

The estimated fair value of the stock options granted in the year ended December 31, 2022 (including but not limited to the exchanged options) was determined utilizing a Black-Scholes option-pricing model at the date of grant. The fair value of the RSUs granted in the year ended December 31, 2022 was determined utilizing the closing price of the Company's common stock on the date of grant. The fair value of the PRSUs granted in the year ended December 31, 2022 was determined utilizing the Monte Carlo simulation method. The Company accounts for all forfeitures when they occur. Ultimately, the actual expense recognized over the vesting period will be for only those shares that vest and are not forfeited.

There were approximately 4.1 million shares available for grant remaining under the 2022 Plan at December 31, 2022. There were approximately 3.6 million shares available for grant remaining under the 2012 Plan at December 31, 2021.

Stock Options and Performance-Based Stock Options

The Company's outstanding option activity for the period from December 31, 2021 through December 31, 2022 is summarized as follows:

	Number of Options (in thousands)	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2021	2,252	$ 50.28	7.2	$ 408
Granted	543	$ 15.04	—	$ —
Exercised	(112)	$ 15.03	—	$ 149
Cancelled/forfeited	(173)	$ 28.42	—	$ —
Expired	(423)	$ 56.88	—	$ —
Outstanding at December 31, 2022	2,087	$ 43.51	7.1	$ 4
Expected to vest	877	$ 21.15	8.6	$ 4
Exercisable	1,210	$ 59.71	6.0	$ —

The aggregate intrinsic value of options is calculated as the difference between the exercise price of the underlying options and the deemed fair value of the Company's common stock for those options that had exercise prices lower than the deemed fair value of the Company's common stock. The weighted-average grant date fair value of options granted in the years ended December 31, 2022, 2021 and 2020 was $9.23, $26.00 and $52.48 per option, respectively. The aggregate intrinsic value of stock options exercised during the years ended December 31, 2022, 2021 and 2020 was $0.2 million, $0.0 million and $0.9 million, respectively. As of December 31, 2022, the total compensation cost related to non-vested option awards not yet recognized is approximately $11.3 million with a weighted average remaining vesting period of 1.17 years.

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

	Years Ended December 31,		
	2022	2021	2020
Volatility	66.4 - 68.9 %	65.2 - 69.3 %	61.9 - 87.1 %
Expected term (in years)	5.5 - 6.0	3.8 - 6.0	5.5 - 6.0
Risk-free rate	1.3 - 4.1 %	0.4 - 1.2 %	0.2 - 1.7 %
Expected dividend yield	— %	— %	— %

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

The following table summarizes the aggregate RSU, RSA and PRSU activity for the year ended December 31, 2022:

	Number of Awards	Weighted Average Grant Date Fair Value
	(in thousands)	
Non-vested awards at December 31, 2021	968	$ 39.58
Granted	880	$ 15.63
Vested	(589)	$ 32.09
Forfeited	(208)	$ 38.71
Non-vested awards at December 31, 2022	1,051	$ 23.90

For the years ended December 31, 2022, 2021 and 2020, the weighted-average grant date fair value of RSUs, RSAs, PRSUs granted was $15.63, $27.49 and $74.68, respectively. The total fair value of RSUs, RSAs and PRSUs that vested during the years ended December 31, 2022, 2021 and 2020 was $18.9 million, $20.6 million and $30.7 million, respectively. As of December 31, 2022, there was $18.3 million of unrecognized compensation expense related to unvested RSUs, RSAs and PRSUs, which is expected to be recognized over a weighted average period of 1.57 years.

During the years ended December 31, 2022, 2021 and 2020, the Company granted a total of 168,600, 176,794 (34,000 forfeited due to termination) and 64,900 PRSUs to certain of the Company's executive officers. The performance criterion for such PRSUs is based on the Total Shareholder Return ("TSR") of the Company's common stock relative to the TSR of the companies comprising the S&P Biotechnology Select Industry Index (the "TSR Peer Group") over a 3-year performance period and is accounted for as a market condition under ASC 718. The TSR for the Company or a member of the TSR Peer Group is calculated by dividing (a) the difference of the ending average stock price minus the beginning average stock price by (b) the beginning average stock price. The beginning average stock price equals the average closing stock price over the one calendar month period prior to the beginning of the performance period, after adjusting for dividends, as applicable. The ending average stock price equals the average closing price over the one calendar month period ending on the last day of the performance period, after adjusting for dividends, as applicable. The Company's relative TSR is then used to calculate the payout percentage, which may range from zero percent (0%) to one hundred and fifty percent (150%) of the target award. The Company utilized a Monte Carlo Simulation to determine the grant date fair

value of such PRSUs. The Company recorded approximately $2.6 million, $0.8 million (net of forfeitures) and $7.8 million (of which $2.9 million related to modifications) of stock-based compensation related to such PRSUs during the years ended December 31, 2022, 2021 and 2020, respectively.

Stock-based compensation expense has been reported in the Company's statements of operations as follows:

	Years Ended December 31,		
	2022	2021	2020
		(in thousands)	
Selling, general and administrative	$ 16,528	$ 22,241	$ 35,572
Research and development	5,361	5,791	12,587
Restructuring		—	1,027
Total stock-based compensation	$ 21,889	$ 28,032	$ 49,186

12. Research and Development Tax Credit

The Company has benefited from the U.K. Small and Medium-sized Enterprise R&D Tax Credit scheme, or the SME scheme, under which it can obtain a tax credit of up to 33.4% of eligible research and development expenses incurred by the Company in the U.K. Eligible expenses generally include employment costs for research staff, consumables, software and certain internal overhead costs incurred as part of research projects.

The Company submitted claims seeking to obtain tax credits for qualifying R&D expenses incurred in the years ended December 31, 2015, 2016 and 2017. In April 2020, the Company received the remaining payment for the 2015 and 2016 claim years of $11.3 million. In June 2020, the Company received a payment of $9.4 million from HMRC for the 2017 claim year. In June 2021, the Company received a payment of $4.2 million from HMRC and made a cash repayment of $0.2 million to the HMRC due to submission of an amended claim.

The claim for 2015 and 2016 was finalized and approved in the quarter ended June 30, 2020, at which time the Company recorded the U.K. research and development tax credit payments received of $22.0 million as a reduction of research and development expense in the consolidated statements of operations.

The claim for 2017 was finalized and approved in the quarter ended June 30, 2021, at which time the Company recorded the U.K. research and development tax credit payments received of $10.7 million as a reduction of research and development expense in the consolidated statements of operations.

The claim for 2018 was finalized and approved in the quarter ended June 30, 2022, at which time the Company recorded the U.K. research and development tax credit payments received of $3.5 million as a reduction of research and development expense in the consolidated statements of operations.

13. Employee Benefit Plans

The Company maintains a defined contribution plan, which is qualified under section 401(k) of the Internal Revenue Code for U.S. employees. Employees may make contributions by withholding a percentage of their salary up to the Internal Revenue Service annual limit of $20,500 and $27,000 in 2022 for employees under 50 years old and employees 50 years old or over, respectively. The Company's matching contribution vests over one year. The Company made payments of approximately $4.4 million, $3.0 million and $2.2 million in matching contributions during the years ended December 31, 2022, 2021 and 2020, respectively.

14. Income Taxes

The components of loss from continuing operations before income taxes for the years ended December 31, 2022, 2021 and 2020 includes the following:

	Years Ended December 31,		
	2022	2021	2020
		(in thousands)	
United States	$ (97,415)	$ (50,063)	$ (127,391)
Foreign	(77,443)	(86,289)	(146,009)
Total	$ (174,858)	$ (136,352)	$ (273,400)

Income tax expense (benefit) from continuing operations differed from the amounts computed by applying the statutory U.S. federal income tax rate of 21% to loss from continuing operations before income taxes as a result of the following:

	Years Ended December 31,		
	2022	2021	2020
		(in thousands)	
Computed "expected" tax benefit	$ (36,720)	$ (28,634)	$ (57,414)
State taxes, net of U.S. federal benefit	—	—	—
U.S. federal tax credits	(3,170)	(4,988)	(5,787)
U.S. GILTI inclusion	8,369	—	—
U.S. federal valuation allowance	(467)	5,996	26,136
Stock-based compensation	4,920	8,784	5,862
Loss on extinguishment of debt	10,567	—	—
Officer compensation	149	496	437
Foreign valuation allowance	13,998	89,743	41,492
Foreign tax rate differences	2,265	(71,622)	(10,830)
Other	89	225	104
Total	$ —	$ —	$ —

The tax effects of temporary differences that give rise to the deferred tax assets and liabilities at December 31, 2022 and 2021 are presented below:

	December 31,	
	2022	2021
	(in thousands)	
Deferred tax assets:		
U.S. federal and state net operating loss and other carryforwards	$ 94,113	$ 174,890
Foreign net operating loss	287,342	304,157
Section 174 R&D Capitalization	12,020	—
Stock compensation	9,527	11,344
Accrued compensation	6,343	4,504
Accrued expense	4,289	4,344
Intangible property	1,631	1,780
Interest limitation	—	10,690
Other	2,686	1,854
Deferred tax assets before valuation allowance	417,951	513,563
Valuation allowance	(417,951)	(469,490)
Total deferred tax assets	—	44,073
Deferred tax liabilities:		
Convertible Notes	—	(44,073)
Total deferred tax liabilities	—	(44,073)
Net deferred tax asset (liability)	$ —	$ —

Net Operating Loss and other carryforwards

As of December 31, 2022, and 2021, the Company had NOLs for U.S. federal income tax purposes of $303.3 million and $669.7 million, respectively, and other carryforwards of $18.2 million and $20.3 million, respectively. The enactment of the Tax Cuts and Jobs Act ("TCJA") modified the ability of companies to utilize NOLs arising in tax years beginning on or after January 1, 2018 by providing that such NOLs may be carried-forward indefinitely and used to offset up to 80 percent of taxable income in any given future year. Existing NOLs that arose in tax years beginning prior to January 1, 2018 were not affected by the TCJA and are generally eligible to be carried-forward for up to 20 years and used to fully offset taxable income in future years. If not utilized, the Company's pre-2018 NOLs and other carryforwards will expire for U.S. federal income tax purposes between 2030 and 2037. The Company also has certain state NOLs in varying amounts depending on the different state tax laws.

As of December 31, 2022, and 2021, the Company had NOLs for foreign income tax purposes of $1.1 billion and $1.2 billion, respectively. Of our $1.1 billion of foreign tax loss carryforwards, all are related to the United Kingdom and may be carried forward indefinitely .

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

Valuation Allowance

At December 31, 2022 and 2021, the Company maintained a full valuation allowance on its deferred tax assets since it has not yet achieved sustained profitable operations. In 2022, the valuation allowance decreased by approximately $74.3 million. This includes decreases of $77.2 million, $2.5 million and $39.5 million for U.S. federal, state and foreign tax, respectively, and an increase of $44.9 million to equity. The decreases primarily relate to the utilization of NOLs to offset the majority of the income tax impact on the sale of the international business to Advanz. The increase to equity primarily relates to the Convertible Notes and the adoption of ASU 2020-06 on January 1, 2022 which reversed the deferred tax liabilities on the portion of the debt balance previously allocated to equity. In 2021, the valuation allowance increased by approximately $55.8 million. This includes an increase of $3.2 million, decrease of $0.5 million and increase of $82.6 million for U.S. federal, state and foreign tax, respectively, and a decrease of $29.5 million to equity. The increase for foreign tax primarily relates to the impact of the United Kingdom tax rate on NOLs which is set to increase from 19% to 25% with effect from April 1, 2023. The decrease to equity primarily relates to the Convertible Notes and the establishment of a deferred tax liability on the debt discount for the 2026 Convertible Secured Notes.

Unrecognized Tax Benefits

At December 31, 2022 and 2021, the Company had no reserves for unrecognized tax benefits.

The Company and its subsidiaries are subject to taxation in the United States and United Kingdom. The Company is subject to U.S. federal and state examinations for 2019 and forward, and 2018 and forward, respectively, and examinations in the United Kingdom for 2019 and forward. However, NOLs are subject to audit in any tax year in which those losses are utilized, notwithstanding the year of origin.

15. Net Loss Per Share

Basic loss per share is computed by dividing net loss attributable to common stockholders (numerator) by the weighted average number of common shares outstanding (denominator) during the period. For the years ended December 31, 2022, 2021 and 2020, the diluted loss per share computations for such periods did not assume the conversion of the Convertible Notes, exercise of stock options or vesting of RSUs or PRSUs as they would have had an anti-dilutive effect on loss per share. The Company utilized the control number concept in the computation of diluted earnings per share. The control number used is net loss from continuing operations. Since the Company had a net loss from continuing operations for all periods presented, no dilutive effect has been recognized in the calculation of income from discontinued operations per share.

The following potentially dilutive securities have been excluded from the computations of diluted weighted average shares outstanding as of December 31, 2022, 2021 and 2020 as the inclusion thereof would have been anti-dilutive:

	December 31,		
	2022	2021	2020
		(in thousands)	
Shares issuable upon conversion of Convertible Notes	19,160	12,362	4,435
Options	2,415	2,615	2,395
Unvested restricted stock units	1,340	1,194	902
Total	22,915	16,171	7,732

16. Commitments and Contingencies

Licenses

The Company acquired a license from a third party to support the portfolio of product candidates. Under the license agreement with Aralez Pharmaceuticals Canada Inc. ("Aralez") the Company has rights to develop and commercialize bezafibrate in the United States. The Company may pay up to $4.5 million upon the achievement of certain milestones, none of which is owed as of December 31, 2022. The Company is obligated to pay royalties to at a mid-single digit percentage of net product sales of such a combination product.

Legal Proceedings

The Company is involved in various disputes, legal proceedings and litigation in the course of its business, including the matters described below and, from time to time, governmental inquiries and investigations and employment and other litigation. These matters, which could result in damages, fines or other administrative, civil or criminal remedies, liabilities or penalties, are often complex and the outcome of such matters is often uncertain. The Company may from time to time enter into settlements to resolve such matters.

Shareholder Litigation

The 2017 Litigation

On September 27, 2017, a purported shareholder class action, initially styled DeSmet v. Intercept Pharmaceuticals, Inc., et al., was filed in the United States District Court for the Southern District of New York, naming the Company and certain of its officers as defendants. On June 1, 2018, the Court appointed lead plaintiffs in the lawsuit, and on July 31, 2018, the lead plaintiffs filed an amended complaint, captioned Hou Liu and Amy Fu v. Intercept Pharmaceuticals, Inc., et al., naming the Company and certain of its current and former officers as defendants. The lead plaintiffs claimed to be suing on behalf of anyone who purchased or otherwise acquired the Company's common stock between June 9, 2016 and September 20, 2017. This lawsuit alleged that material misrepresentations and/or omissions of material fact were made in the Company's public disclosures during that period, in violation of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Rule 10b-5 promulgated thereunder. The alleged improper disclosures relate to statements regarding Ocaliva dosing and use, and pharmacovigilance-related matters, as well as the Company's operations, financial performance, and prospects. The plaintiffs sought unspecified monetary damages on behalf of the putative class, an award of costs and expenses, including attorney's fees, and rescissory damages. On September 14, 2018, the Company filed a motion to dismiss the amended complaint. On March 26, 2020, the Court granted the Company's motion to dismiss the amended complaint in its entirety, and on March 27, 2020 the Court entered judgment in favor of the Company. On May 8, 2020, the plaintiffs filed a motion to set aside the judgment and grant leave to file a second amended complaint. On September 9, 2020, the Court denied the plaintiffs' motion, finding that the proposed second amended complaint did not cure the deficiencies identified in the amended complaint. On October 9, 2020, the plaintiffs filed a notice of appeal to the United States Court of Appeals for the Second Circuit and on January 25, 2021, the plaintiffs filed an appellate brief challenging the March 27, 2020 judgment, the September 9, 2020 judgment, and other court orders. On April 23, 2021, the Company filed a response brief in the Second Circuit appellate proceeding. On May 14, 2021, the plaintiffs filed a reply brief. On December 9, 2021, oral argument was held in the Second Circuit. On June 16, 2022, the Second Circuit entered a summary order affirming the order of the District Court dated September 9, 2020.

Separately, on December 1, 2017, a purported shareholder demand was made on the Company based on substantially the same allegations as those set forth in the securities case above. Also, on January 5, 2018, a follow-on derivative suit, styled Davis v. Pruzanski, et al., was filed in New York state court by shareholder Gregg Davis based on substantially the same allegations as those set forth in the securities case above. The derivative litigation was stayed pending the exhaustion of all appeals relating to the dismissal of the securities case. Following exhaustion of such appeals, on October 7, 2022,

the parties stipulated to and agreed to a discontinuance of the derivative suit. On February 7, 2023, the court marked the case as disposed of due to the discontinuance.

Patent Litigation

The Company has received paragraph IV certification notice letters from seven generic drug manufacturers indicating that each such manufacturer submitted to the FDA an Abbreviated New Drug Application ("ANDA") seeking approval to manufacture and sell a generic version of the Company's 5 mg and 10 mg dosage strengths of Ocaliva® (obeticholic acid) for PBC prior to the expiration of certain patents listed for Ocaliva in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book").

The seven generic drug manufacturers and when we received their initial paragraph IV certification notices are as follows: (1) Apotex Inc. ("Apotex") (July 2020), (2) Lupin Limited ("Lupin") (July 2020), (3) Amneal Pharmaceuticals of New York, LLC, as U.S. agent for Amneal EU Limited (collectively, "Amneal") (July 2020), (4) Optimus Pharma Pvt Ltd ("Optimus") (July 2020), (5) MSN Pharmaceuticals Inc. and MSN Laboratories Private Limited (collectively, "MSN") (July 2020), (6) Dr. Reddy's Laboratories, Inc., and Dr. Reddy's Laboratories, Ltd. (collectively, "Dr. Reddy's") (December 2020), and (7) Zenara Pharma Private Limited ("Zenara") (August 2022).

Each paragraph IV certification notice alleged that the challenged Orange Book patents were invalid, unenforceable, and/or would not be infringed by the commercial manufacture, use, or sale of the generic products described in the generic manufacturer's respective ANDA. In each case, within 45 days of receipt of the paragraph IV certification notice, the Company initiated a patent infringement suit against the generic manufacturer in the United States District Court for the District of Delaware.

We entered into settlement agreements with Apotex, Lupin, Amneal, Optimus, MSN and Dr. Reddy's. Those settlements fully resolved the patent infringement case in the United States District Court for the District of Delaware that was scheduled for trial on February 27, 2023, and the case was terminated by the Court. Separate patent litigation against Zenara remains pending in the District of Delaware, with trial scheduled for July 22, 2024. Under the Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Act"), the FDA cannot grant final approval of the Zenara ANDA before the earlier of February 8, 2025, or a court decision in its favor. Under the terms of the six settlement agreements, the Company granted each of the manufacturers a non-exclusive, non-sublicensable, non-transferable, royalty-free license to commercialize a generic version of Ocaliva in the United States commencing on a specified date, or earlier under certain circumstances. The earliest such specified date agreed to is September 1, 2031 (for Apotex).

These patent proceedings are costly and time-consuming, and successful challenges to the Company's patents or other intellectual property rights could result in the Company losing those rights in the relevant jurisdiction, and could allow third parties to use the Company's proprietary technologies without a license from the Company or its collaborators. While the Company intends to vigorously defend and enforce its intellectual property rights protecting Ocaliva, the Company can offer no assurances regarding when patent lawsuits such as the Zenara lawsuit will be decided, which side will prevail, or whether a generic equivalent of Ocaliva could be approved and enter the market before the expiration of the Company's patents without license from the Company.

17. Quarterly Financial Data (unaudited)

The following table summarizes the unaudited quarterly financial data for the years ended December 31, 2022 and 2021, presented for continuing and discontinued operations.

	Quarters Ended				
	March 31,	June 30,	September 30,	December 31,	Total
	(in thousands, except for per share amounts)				
2022					
Total revenue	$ 59,146	$ 71,757	$ 77,588	$ 77,219	$ 285,710
Operating loss	$ (26,428)	$ (13,041)	$ (9,838)	$ (18,909)	$ (68,216)
Loss from continuing operations	$ (33,436)	$ (20,095)	$ (103,784)	$ (17,543)	$ (174,858)
Income (loss) from discontinued operations	$ 16,151	$ 12,567	$ 371,237	$ (3,281)	$ 396,674
Net income (loss)	$ (17,285)	$ (7,528)	$ 267,453	$ (20,824)	$ 221,816
Net loss from continuing operations per share - basic and diluted (1)	$ (1.13)	$ (0.68)	$ (3.03)	$ (0.42)	$ (5.17)
Net income (loss) from discontinued operations per share - basic and diluted (1)	$ 0.54	$ 0.42	$ 10.83	$ (0.08)	$ 11.72
Net income (loss) per common share - basic and diluted (1)	$ (0.58)	$ (0.25)	$ 7.80	$ (0.50)	$ 6.56
2021					
Total revenue	$ 57,299	$ 68,178	$ 66,640	$ 68,633	$ 260,750
Operating loss	$ (38,594)	$ (13,153)	$ (19,483)	$ (29,176)	$ (100,406)
Loss from continuing operations	$ (49,699)	$ (25,087)	$ (16,970)	$ (44,596)	$ (136,352)
Income from discontinued operations	$ 9,279	$ 13,994	$ 13,338	$ 8,315	$ 44,926
Net loss	$ (40,420)	$ (11,093)	$ (3,632)	$ (36,281)	$ (91,426)
Net loss from continuing operations per share - basic and diluted (1)	$ (1.50)	$ (0.76)	$ (0.53)	$ (1.51)	$ (4.28)
Net income from discontinued operations per share - basic and diluted (1)	$ 0.28	$ 0.42	$ 0.42	$ 0.28	$ 1.41
Net loss per common share - basic and diluted (1)	$ (1.22)	$ (0.33)	$ (0.11)	$ (1.23)	$ (2.87)

1) Basic and diluted net income (loss) per common share is computed indepdently for each of the quarters presented. Therefore, the sum of the quarterly basic and diluted net income (loss) per common share may not equal annual basic and diluted net income (loss) per common share.

Exhibit 21.1

SUBSIDIARY OF THE REGISTRANT

Name	Jurisdiction of Incorporation or Organization
Intercept Pharma Europe Ltd.	England and Wales

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the registration statements (Nos. 333-184810, 333-188064, 333-206247, 333-217863, 333-226405, 333-233248, 333-248083, 333-259892, and 333-268727) on Form S-8 and (Nos. 333-194974 and No. 333-217861) on Form S-3 of our reports dated March 2, 2023, with respect to the consolidated financial statements of Intercept Pharmaceuticals, Inc. and the effectiveness of internal control over financial reporting.

/s/ KPMG LLP

New York, New York
March 2, 2023

Exhibit 31.1

CERTIFICATION

I, Jerome Durso, certify that:

1. I have reviewed this Annual Report on Form 10-K of Intercept Pharmaceuticals, Inc.;

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

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

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

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

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

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

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

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

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

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

Date: March 2, 2023

/s/ Jerome Durso
Jerome Durso
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

I, Andrew Saik, certify that:

1. I have reviewed this Annual Report on Form 10-K of Intercept Pharmaceuticals, Inc.;

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

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

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

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

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

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

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

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

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

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

Date: March 2, 2023

/s/ Andrew Saik
Andrew Saik
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Jerome Durso, President and Chief Executive Officer of Intercept Pharmaceuticals, Inc. (the "Company"), and Andrew Saik, Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

(1) The Company's Annual Report on Form 10-K for the year ended December 31, 2022 to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

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

Dated: March 2, 2023

/s/ Jerome Durso
Jerome Durso
President and Chief Executive Officer
(Principal Executive Officer)

Dated: March 2, 2023

/s/ Andrew Saik
Andrew Saik
Chief Financial Officer
(Principal Financial Officer)

A signed original of this written statement required by Rule 13a-14(b) of the Exchange Act and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350) has been provided to Intercept Pharmaceuticals, Inc. and will be retained by Intercept Pharmaceuticals, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.

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